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## Organic Reactions

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### PREFACE TO THE SERIES

In the course of nearly every program of research in organic chemistry the investigator finds it necessary to use several of the better-known synthetic reactions. To discover the optimum conditions for the application of even the most familiar one to a compound not previously subjected to the reaction often requires an extensive search of the literature; even then a series of experiments may be necessary. When the results of the investigation are published, the synthesis, which may have required months of work, is usually described without comment. The background of knowledge and experience gained in the literature search and experimentation is thus lost to those who subsequently have occasion to apply the general method. The student of preparative organic chemistry faces similar difficulties. The textbooks and laboratory manuals furnish numerous examples of the application of various syntheses, but only rarely do they convey an accurate conception of the scope and usefulness of the processes.

For many years American organic chemists have discussed these problems. The plan of compiling critical discussions of the more important reactions thus was evolved. The volumes of Organic Reactions are collections of chapters each devoted to a single reaction, or a definite phase of a reaction, of wide applicability. The authors have had experience with the processes surveyed. The subjects are presented from the preparative viewpoint, and particular attention is given to limitations, interfering influences, effects of structure, and the selection of experimental techniques. Each chapter includes several detailed procedures illustrating the significant modifications of the method. Most of these procedures have been found satisfactory by the author or one of the editors, but unlike those in Organic Syntheses they have not been subjected to careful testing in two or more laboratories. When all known examples of the reaction are not mentioned in the text, tables are given to list compounds which have been prepared by or subjected to the reaction. Every effort has been made to include in the tables all such compounds and references; however, because of the very nature of the reactions discussed and their frequent use as one of the several steps of syntheses in which not all of the intermediates have been isolated, some instances may well have been missed. Nevertheless, the investigator will be able

to use the tables and their accompanying bibliographics in place of most or all of the literature search so often required.

Because of the systematic arrangement of the material in the chapters and the entries in the tables, users of the books will be able to find information desired by reference to the table of contents of the appropriate chapter. In the interest of economy the entries in the indices have been kept to a minimum, and, in particular, the compounds listed in the tables are not repeated in the indices.

The success of this publication, which will appear periodically, depends upon the cooperation of organic chemists and their willingness to devote time and effort to the preparation of the chapters. They have manifested their interest already by the almost unanimous acceptance of invitations to contribute to the work. The editors will welcome their continued interest and their suggestions for improvements in *Organic Reactions*.

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### CHAPTER 1

### THE CLEAVAGE OF NON-ENOLIZABLE KETONES WITH SODIUM AMIDE. THE HALLER-BAUER REACTION

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### INTRODUCTION

In this chapter the Haller-Bauer reaction is defined as the action of sodium amide on a non-enolizable ketone earsing cleavage of a carbon to carbon bond and resulting in the formation of an amide and a hydrocarbon.

$$R-C-R'$$
  $\xrightarrow{NaNH_2}$   $RCONH_2 \div R'H$ 

Textbook definitions of the Haller-Bauer reaction have limited it to the alkylation of ketones in which sodium amide acts as a condensing agent<sup>1,2</sup> or have considered it a combination of the alkylation and cleavage reactions.<sup>3</sup>

The cleavage of ketones by sodium amide was discovered in 1906 by Semmler<sup>4</sup> in connection with his investigations of the structure of fenchone. Suspecting that fenchone contained no  $\alpha$ -hydrogen atoms, Semmler chose sodium amide as a reagent that might effect a cleavage without causing rearrangement of the molecule. As a result, the sodio derivative of fencholic acid amide was obtained. He did not explore the potentialities of the reaction. This was done by Haller and Bauer,<sup>5</sup> who in 1908 reported the isolation of benzamide after the treatment of benzophenone with sodium amide in boiling benzene or tolucne and who followed this observation with an extended study of the reaction.

A modification of the Haller-Bauer reaction involving the use of a fused eutectic mixture of sodium and potassium amides<sup>6</sup> has been applied to certain alicyclic and bicyclic terpenoid ketones as well as to some amides. The earbonyl group was completely climinated from these compounds. For example, fenchone was cleaved to 1-methyl-3-isopropyleyclopentane, and 1-benzoylpiperidine gave rise to benzene and piperidine.

#### MECHANISM

On the basis of their early experiments, Haller and Baner proposed a mechanism for the reaction of sodium amide with benzophenone which involved a preliminary addition to the ketone.<sup>5</sup> The "sodium salt of

<sup>&</sup>lt;sup>1</sup> Cohen, Organic Chemistry for Advanced Students, I, 4th ed., p. 217, Longmans, Green and Co., New York, 1924.

<sup>&</sup>lt;sup>2</sup> Degering, An Outline of Organic Chemistry, 4th ed., p. 321, Barnes and Noble, 1941.

<sup>3</sup> The Merck Index, 6th ed., p. 1055, Merck and Co., Rahway, N.J., 1952.

<sup>&</sup>lt;sup>4</sup> Semmler, Ber., 39, 2577 (1906).

<sup>&</sup>lt;sup>5</sup> Haller and Bauer, Compt. rend., 147, 824 (1908).

<sup>&</sup>lt;sup>6</sup> Freidlin, Balandin, and Lebedova, Bull. Acad. Sci. U.R.S.S., Classe sci. chim., 1941, 167 [C. A., 37, 3749 (1943)].

diphenylaminocarbinol" (I) thus formed could be isolated as a crystalline

$$\begin{array}{c} \text{ONa} \\ \text{C}_{6}\text{H}_{5}\text{COC}_{6}\text{H}_{5} + \text{NaNH}_{2} \rightarrow \text{C}_{6}\text{H}_{5} \\ \text{C}_{-}\text{C}_{6}\text{H}_{5} \\ \text{NH}_{2} \\ \text{I} \\ \\ \text{C}_{6}\text{H}_{5} - \text{C}_{-}\text{C}_{6}\text{H}_{5} + \text{H}_{2}\text{O} \rightarrow \text{C}_{6}\text{H}_{5}\text{CONH}_{2} + \text{C}_{6}\text{H}_{6} + \text{NaOH} \\ \text{NH}_{2} \\ \end{array}$$

product. Upon treatment with water it gave rise to benzamide and benzene. In 1922 Haller published a review article and repeated his ideas on the mechanism of the reaction.

Schönberg in 1924 and 1925 described his researches on the action of sodium amide on diaryl ketones.<sup>8,9</sup> His observations with benzophenone were in agreement with those of Haller and Bauer; his interpretation of the reaction, however, differed from theirs as far as the decomposition of the adduct I was concerned. It was Schönberg's view that the addition product I undergoes thermal cleavage in boiling benzene or toluene to furnish benzene and the sodio derivative of benzamide,<sup>10</sup> which can be isolated from the reaction mixture. Treatment with water hydrolyzes this latter sodio derivative to benzamide.

$$C_6H_5CONHNa + H_2O \rightarrow C_6H_5CONH_2 + NaOH$$

Further evidence to support this mechanism was provided by the reaction of p-phenylbenzophenone with sodium amide. When these materials were heated under refluxing conditions in dry toluene and the solid so formed was removed by filtration, biphenyl was isolated from the filtrate. As both the hydrocarbon and the sodio derivative of the amide were formed in the absence of water it was evident that water was not necessary for the formation of the hydrocarbon. Lea and Robinson<sup>11</sup> have carried out additional experiments on the action of sodium amide

<sup>7</sup> Haller, Bull. soc. chim. France, [4] 31, 1117 (1922).

<sup>8</sup> Schönberg, Abelsdorff, Kirchrath, Malchov, and Rosen, Ann., 436, 205 (1924).

<sup>9</sup> Schönberg, Ber., 58, 580 (1925).

<sup>10</sup> Curtius, Ber., 23, 3038 (1890).

<sup>11</sup> Lea and Robinson, J. Chem. Soc., 1926, 2351.

on unsymmetrical benzophenones. Their description of the reaction mechanism is in full agreement with that of Schönberg.

A modern interpretation of the reaction might be written as follows:

$$\begin{array}{c} O^{-} \\ \downarrow \\ RCOR' + NH_{2}^{-} = R - C - R' = R^{-} + H_{2}NCOR' \rightarrow RH + \overline{(HNCOR')} \\ \downarrow \\ NH_{2} \end{array}$$

The direction of cleavage depends upon the relative electronegativities of R and R'. If R' in the ketone, RCOR', is more strongly electron repelling than R the primary product is R'CONH<sub>2</sub>.

The mechanism suggested by Freidlin<sup>6</sup> for the modification of the Haller-Bauer reaction in which a fused entectic mixture of sodium and potassium amides reacts with a ketone or an amide is given below. Cleavage occurs to eliminate the carbonyl group with the formation of metal cyanamides.

#### SCOPE AND LIMITATIONS

The Haller-Bauer reaction has been applied to many non-enolizable ketones<sup>12</sup> and with certain classes of these compounds has considerable synthetic utility. It is one of the few general methods for the synthesis of tertiary carboxamides, compounds which are useful as intermediates for tertiary carboxylic acids or tertiary carbinamines. By hydrolysis of the amides, <sup>13</sup> many tertiary carboxylic acids have been made available, and an even less accessible class of compounds, the tertiary carbinamines, can be formed by application of the Hofmann, Schmidt, and Curtius reactions to the amides or acids. <sup>14</sup>

 $<sup>^{12}</sup>$  A few ketones having an  $\alpha$ -hydrogen atom have been cleaved by sodium amide during attempted alkylation. Some of these cleavages are considered on pp. 8 and 12; all are cited in Table I.

<sup>&</sup>lt;sup>13</sup> Sperber, Papa, and Schwenk, J. Am. Chem. Soc., 70, 3091 (1948).

<sup>14</sup> Organic Reactions, Vol. III, Chapters 7, 8, and 9, John Wiley & Sons, New York, 1946.

### The Cleavage of Aliphatic or Alicyclic Phenyl Ketones (Table I)

The most important application of the Haller-Bauer reaction is the eleavage of aliphatic or alicyclic phenyl ketones. Broadly, the eleavage occurs in such a way as to produce the tertiary carboxamides. For example,  $\alpha,\alpha$ -dimethylpropiophenone when heated in benzene under refluxing conditions with sodium amide affords a nearly quantitative yield of pivalamide. Similarly, 1-methylcyclohexyl phenyl ketone under the same conditions readily forms 1-methylcyclohexanecarboxamide in 88% yield. Since the starting ketones in general are rather easily obtained, the reaction has found considerable application.

When two of the substituents (for example, R and R') of a trialkylaeeto-phenone II are methyl, the third (R") may be increased in size to  $C_{18}$  without interfering with the normal direction of the reaction. On the

other hand, as R and R' increase in size and complexity, the yields of trialkylaeetamides fall off rapidly and the amount of benzamide increases. This effect was studied in detail by restricting one alkyl group to methyl or ethyl and progressively increasing in size the other two.15 No difficulty was experienced in the preparation of variously branched amides containing up to ten earbon atoms. However, in II, where R, R', and R" total eleven carbon atoms, certain irregularities became evident and more benzamide resulted. For example, α-methyl-α-n-butyl-n-hexamide and α-ethyl-α-n-propyl-n-hexamide were formed readily. On the other hand, α-methyl-α-ethyl-n-octamide was obtained in an impure state while α,α-diethylheptamide could not be isolated. With a total of twelve or more carbon atoms in the three substituent groups, the molecules exhibited even greater variation from the normal direction of cleavage. investigators concluded that failure of the method might be expected with alkyl phenyl ketones of relatively low molecular weight where the three substituents are highly complex.

The results of these workers may be explained partly on the basis of steric hindrance: the more complex the branching about the carbonyl group, the less successful is the cleavage. Recovery of some starting ketone from the reaction mixture is possible with such compounds. However, the isolation of increasing amounts of benzamide indicates that some attack on the carbonyl group occurs.

<sup>15</sup> Carter and Slater, J. Chem. Soc., 1946, 130.

The application of Newman's "Rule of Six" to account for the steric effects of branching about the carbonyl group is only partly satisfactory. The results are neither strikingly in agreement nor strikingly in disagreement with the rule.

The cleavage of alicyclic phenyl ketones by their reaction with sodium amide  $^{17-21}$  follows the direction reported for alkyl phenyl ketones. Good yields of the expected 1-alkyl alicyclic carboxamides were obtained with little evidence of benzamide where the alkyl substituent (R) was methyl, ethyl, n-propyl, isopropyl, or n-butyl.

$$(\widehat{\operatorname{CH}_2)_n}\widehat{\operatorname{C}}^{\operatorname{R}}_{\operatorname{COC}_6\operatorname{H}_5}$$

Anomalous results were reported with 1-methylcyclopropyl phenyl ketone, which furnished benzamide and no 1-methylcyclopropanecarbox-amide.<sup>17</sup> On the other hand, replacement of methyl by benzyl changed the direction of cleavage and 1-benzylcyclopropanecarboxamide was obtained readily. This cleavage of 1-benzylcyclopropyl phenyl ketone in the expected manner was confirmed by the hydrolysis of the amide and identification of the 1-benzylcyclopropanecarboxylic acid.<sup>20</sup>

Diketones of type III provide an excellent source of  $\alpha, \alpha, \alpha', \alpha'$ -tetraalkyldiamides. The diketones, where R is methyl and n has been varied from 3 to 14, have been converted to diamides.<sup>22–24</sup>

The reaction also proceeds in the expected manner with diketones such as IV, synthesized by use of a dihalide containing a benzene nucleus. The corresponding *ortho* and *meta* derivatives were also prepared.<sup>25</sup>

- <sup>16</sup> Newman, J. Am. Chem. Soc., 72, 4783 (1950).
- <sup>17</sup> Haller and Benoist, Ann. chim. Paris, [9] 17, 25 (1921).
- 16 Wash, Shive, and Lochte, J. Am. Chem. Soc., 63, 2975 (1941).
- 19 Hamlin and Freifelder, J. Am. Chem. Soc., 75, 369 (1953).
- <sup>20</sup> Piehl and Brown, J. Am. Chem. Soc., 75, 5023 (1953).
- <sup>21</sup> Hamlin and Biermacher, J. Am. Chem. Soc., 77, 6376 (1955).
- <sup>22</sup> Haller and Bauer, Compt. rend., 152, 1638 (1911).
- <sup>23</sup> Adams and Anderson, J. Am. Chem. Soc., 73, 136 (1951).
- <sup>24</sup> Leonard and Mader, J. Am. Chem. Soc., 72, 5388 (1950).
- <sup>25</sup> Dumesnil, Ann. chim. Paris, [9] 8, 70 (1917).

An interesting secondary reaction is encountered in a series of 1,1-dialkyl-3-butenyl phenyl ketones (V). These ketones on treatment with sodium amide yield unsaturated amides which eyelize to the corresponding pyrrolidones (VI). Brown and van Guliek<sup>26</sup> conclusively proved that for

3,3,5-trimethyl-2-pyrrolidone the reaction takes the course proposed by Haller and Bauer,<sup>27</sup> viz., the 2,2-dimethyl-4-pentenamide arising from the sodium amide cleavage of 1,1-dimethyl-3-butenyl phenyl ketone will cyclize under basic conditions.

Several 5-methyl-3,3-dialkyl-2-pyrrolidones have been prepared by this method, and the reaction is considered to be general.<sup>28</sup>

Most aralkyl and heterocyclic-alkyl phenyl ketones on treatment with sodium amide give the expected substituted alkylacetamides (Table I). However,  $\alpha,\alpha$ -dimethyl- $\gamma,\delta$ -epoxybutyl phenyl ketone is not attacked.<sup>29</sup>

The synthetic utility of the Haller-Bauer reaction is limited by the unavailability of the starting ketones. The simpler ketones are readily obtained by the alkylation of various acetophenones by conventional

<sup>&</sup>lt;sup>26</sup> Brown and van Guliek, J. Am. Chem. Soc., 77, 1092 (1955)

<sup>27</sup> Haller and Bauer, Compt. rend., 158, 1086 (1914).

<sup>28</sup> Haller and Bauer, Compt. rend., 160, 541 (1915).

<sup>29</sup> Ramart-Lucas and Haller, Compt. rend., 158, 1302 (1914).

methods. The introduction of the third group into ketones of high molecular weight is restricted by steric effects. Such alkylations become progressively more difficult as the size of the entering group becomes larger; this is a major drawback to the use of the method for synthesis of acids containing a quaternary carbon atom.<sup>30</sup> Thus, it is impossible to methylate  $\omega, \omega$ -di-n-decylacetophenone. This barrier to the synthesis of trialkylacetophenones in which two substituents are long chain can be obviated by introducing the small group first into a higher homolog of acetophenone and then replacing the tertiary hydrogen by a long-chain alkyl group.<sup>15</sup>

Attempts to introduce an alkyl group in the tertiary position of an alieyclic phenyl ketone sometimes gave anomalous results. Alkylation of 2-methyleyclopentyl phenyl ketone was usually normal, but if the ketone was allowed to react with sodium amide in boiling xylene and then treated with isopropyl iodide a mixture of 2-methylcyclopentanecarboxamide, N-isopropyl-2-methylcyclopentanecarboxamide, and the isopropyl ether of the enol form of the parent ketone resulted. 18,19 Cleavage of this

ketone, containing an α-hydrogen atom, was occurring in place of alkylation. The cleavage of eyelohexyl phenyl ketone by sodium amide resulted in a 1% yield of cyclohexaneearboxamide. Similarly cyclopropyl phenyl ketone with sodium amide in boiling benzene gave a 42% yield of cyclopropanecarboxamide as well as a small amount (2%) of benzamide. These results could not be repeated and do not coincide with those previously reported that, with sodium amide in moist benzene, benzamide was the only product isolated.<sup>17</sup>

### The Cleavage of Aliphatic Ketones (Table II)

Symmetrically substituted acetones react with sodium amide to form the predicted tertiary earboxamide and trialkylated methane.<sup>31</sup> Thus hexamethylacetone gives an excellent yield of pivalamide by this method.

<sup>30</sup> Birch and Robinson, J. Chem. Soc., 1942, 488.

<sup>31</sup> Haller and Bauer, Compt. rend., 150, 664 (1910).

On the other hand, a mixture of the four possible products (two amides and two hydrocarbons) is obtained from 2,2,4,4-tetramethyl-3-hexanone (VII).

Although substituted acetones may furnish a mixture of two possible amides and two hydrocarbons, one direction of cleavage may predominate. 2,2,4,4-Tetramethyl-5-phenyl-3-pentanone (VIII) cleaves exclusively to pivalamide and isobutylbenzene;  $^{32}$  4,4-diethyl-2,2-dimethyl-3-hexanone (IX) when treated with sodium amide at the boiling point of xylene forms pivalamide and  $\alpha,\alpha,\alpha$ -triethylacetamide in a 5-to-1 ratio.  $^{31}$ 

An additional limitation to the practical use of the reaction with aliphatic ketones is encountered when the substituents are highly branched. For instance, the ketone X is inert to the action of sodium amide under vigorous conditions.<sup>32</sup> Since in such cases the starting ketone is recovered, the failure of the reaction is possibly attributable to steric hindrance about the carbonyl group.

### The Cleavage of Diaryl Ketones (Table III)

Diaryl ketones are readily attacked by sodium amide. If symmetrically substituted they can yield only one amide and one hydrocarbon. Unsymmetrical diaryl ketones in which the substituents cause one aromatic nucleus to be much more strongly electron donating than the other give predominantly one amide and one hydrocarbon.

From the large number of diaryl ketones falling between these two extremes, four possible products, two amides and two hydrocarbons, are formed in varying amounts. Only the first two types of diaryl ketones are useful for the preparation of amides.

Schönberg<sup>8,9</sup> and Lea and Robinson<sup>11</sup> cleaved a variety of unsymmetrical diaryl ketones and determined the comparative yields of the various

<sup>32</sup> Haller and Bauer, Ann. chim. Paris, [9] 1, 5 (1914).

benzamides or benzoic acids. They and, later, de Ceuster<sup>33</sup> drew the conclusion illustrated below that the presence of an electron-supplying group favors cleavage to produce the substituted benzamide. The same substituent in an *ortho* position results in almost complete cleavage to yield the unsubstituted benzamide; e.g., 2-methoxybenzophenone furnishes benzamide almost exclusively.

The effect of conditions upon the Haller-Bauer reaction may be illustrated by the action of sodium amide on  $\alpha$ -naphthyl phenyl ketone. The contract of the property of the property of the contract of the c

Examples of the action of sodium amide on cyclized aromatic ketones are few. Fluorenone has been shown to yield o-phenylbenzamide in the expected manner.<sup>25,36</sup> However, anthraquinone was recovered unchanged after treatment with sodium amide.<sup>29</sup>

<sup>&</sup>lt;sup>33</sup> De Ceuster, Natuurw. Tijdschr. Belg., 14, No. 3-6, 188 (1932) [C. A., 26, 4323 (1932)]
Chem. Zentr., 1932, II, 1296].

<sup>34</sup> Lucas, Ann. chim. et phys., [8] 17, 127 (1909).

<sup>35</sup> Haller and Bauer, Compt. rend., 147, 824 (1908).

<sup>36</sup> Haller and Bauer, Ann. chim. et phys., [8] 16, 145 (1909).

### The Cleavage of Alicyclic Ketones (Table IV)

Following the first use of the Haller-Bauer reaction on fenchone, sodium amide cleavage was used in clucidation of the structure of certain terpenes related to camphor.<sup>4</sup> Several dialkylcamphors were cleaved by sodium amide to the corresponding dialkylcampholamides.<sup>27,38</sup> Each ketone cleaved in one direction and gave good yields of 1,2,2-trimethyl-3-alkyleyelopentaneearboxamide.

Symmetrically substituted cyclic ketones react with opening of the ring and give rise to one product only, an aliphatic carboxamide. Thus, with 2,2,5,5-tetramethyleyelopentanone<sup>29</sup> (XI) cleavage proceeds as

indicated. Unsymmetrically substituted cyclopentanones, however, give a mixture of two aliphatic carboxamides, thereby limiting the usefulness of the reaction. Cyclohexanones are reported? to be very resistant to the action of sodium amide.

### The Action of Sodium Amide upon Miscellaneous Carbonyl Compounds (Table V)

Other types of earbonyl compounds have been treated with sodium amide under similar conditions. Aromatic aldehydes undergo the Cannizzaro reaction to yield the corresponding alcohol and acid. 1997. Benzil and substituted benzils give a typical benzilic acid rearrangement of the compoundation of accomplete the compoun

reacts in the following manner.43 The mixture of isomers was separated and each isomer was treated with sodium amide. The lower-melting isomer undergoes the Haller-Bauer reaction and hence was assigned structure XII.43,44 The higher-melting isomer that has an α-hydrogen does not undergo cleavage with sodium amide and hence could be designated by structure XIII or by an analogous structure in which the double bond is in another position in the ring. A parallel reaction sequence has been established for 1,7-diphenylheptane-1,7-dione.45

2,4-Dimethyl-1,3,5-triphenylpentane-1,5-dione (XIV), which contains  $\alpha$ -hydrogen atoms, was cleaved with sodium amide in what appears to be a reverse Michael reaction.46

### RELATED SYNTHETIC PROCESSES

Synthesis of Tertiary Carboxylic Acids. The principal alternative methods for synthesis of tertiary carboxylic acids (trisubstituted acetic acids) are briefly surveyed here. Most of the literature resulted from efforts to synthesize phthioic acid (ethyl-n-decyl-n-dodecylacetic acid) and similar structures. 30,47,48

The aliphatic nitriles may be alkylated to the corresponding trialkylacetonitriles,49 which may be hydrolyzed first to the amides with 80% sulfuric acid and finally to the acids. Although the difficulty of hydrolysis

<sup>43</sup> Bauer and Haller, Compt. rend., 156, 1470 (1913).

<sup>44</sup> Bauer and Haller, Compt. rend., 156, 1684 (1913).

<sup>45</sup> Bauer, Ann. chim. Paris, 1, 343 (1914).

<sup>46</sup> Bauer and Haller, Compt. rend., 158, 1680 (1914).

<sup>47</sup> Polgar and Robinson, J. Chem. Soc., 1943, 615.

<sup>48</sup> Hook and Robinson, J. Chem. Soc., 1944, 152.

<sup>49</sup> Ziegler and Ohlinger, Ann., 495, 84 (1932).

of the nitriles is a serious limitation of the method, a series of trialkylacetonitriles in which the alkyl groups contain as many as seven carbon atoms has been successfully hydrolyzed.<sup>13</sup>

Trialkylacetic acids have also been prepared by the carbonation of t-alkylmagnesium chlorides. This method suffers from many disadvantages, principally the difficulty of forming Grignard reagents from tertiary alkyl halides of high molecular weight.

α-Alkylation of esters can be effected by means of sodium triphenylmethyl and an alkyl halide.<sup>51</sup> However, the separation of unreacted disubstituted acetic acids or esters necessitates a tedious purification.

To a limited degree, the Favorski rearrangement of  $\alpha$ -halogenated ketones can be used in the synthesis of tertiary carboxylic acids. <sup>52–54</sup> However, wherever the R groups become large or complex only metathesis occurs in the first step.

Synthesis of Tertiary Carbinamines. Synthesis of amines in which the amino group is attached to a tertiary carbon atom has been reported in only isolated instances, and in most of them the simplest member of the series, t-butylamine, was the material prepared.

A group of tertiary carbinamines has been synthesized by reaction of certain nitriles with a Grignard reagent.<sup>55</sup> In this fashion, alkoxyalkyl, aralkyl, or alkenyl cyanides on treatment with allylmagnesium bromide formed tertiary carbinamines in which two of the substituent groups were allyl. Hydrogenation yielded the corresponding propyl compounds.

Tertiary nitriles, prepared by alkylation of primary nitriles, <sup>49</sup> can be hydrolyzed to the corresponding amides. After conversion to the isocyanates by the Hofmann method, tertiary carbinamines can be obtained by hydrolysis.

The most important innovation in synthetic methods for the preparation of such amines is that developed by Ritter and co-workers,  $^{56,57}$  in which treatment of an alkene with a nitrile in the presence of concentrated sulfuric acid produces excellent yields of amides of t-carbinamines.

<sup>50</sup> Whitmore and Badertscher, J. Am. Chem. Soc., 55, 1559 (1933).

<sup>&</sup>lt;sup>51</sup> Hudson and Hauser, J. Am. Chem. Soc., 62, 2457 (1940).

<sup>52</sup> Marker and Wagner, J. Am. Chem. Soc., 64, 216 (1942).

<sup>&</sup>lt;sup>23</sup> Aston, Clarke, Burgess, and Greenburg, J. Am. Chem. Soc., 64, 300 (1942).

<sup>&</sup>lt;sup>54</sup> Plattner, Heusser, and Boyce, Helv. Chim. Acta, 31, 603 (1948).

<sup>55</sup> Henze, Allen, and Leslie, J. Am. Chem. Soc., 65, 87 (1943).

<sup>&</sup>lt;sup>14</sup> Ritter and Minieri, J. Am. Chem. Soc., 70, 4045 (1948).

<sup>&</sup>lt;sup>17</sup> Ratter and Kalish, J. Am. Chem. Soc., 70, 4048 (1948).

When sodium eyanide is used as the nitrile, the N-alkylformamides formed can be hydrolyzed readily to the desired amines. A tertiary alcohol can be substituted for the alkene.

t-Butylamine has been prepared in 73% yield by the reaction of t-butylamagnesium chloride with methoxyamine.<sup>58</sup>

### EXPERIMENTAL CONDITIONS

The Haller-Bauer reaction is carried out by heating a non-enolizable ketone in an inert solvent in the presence of sodium amide. Benzene, toluene, and xylene have been used successfully. In certain instances where reaction has failed in benzene or toluene under refluxing conditions, the higher boiling temperature of xylene has led to success.

Although the quantities of sodium amide employed by various workers have varied, the use of two moles of this reagent for each carbonyl group to be cleaved is customary. Sodium amide now may be purchased, but usually it is freshly prepared in the vessel in which the reaction is to be carried out. Suitable directions for the preparation of sodium amide are found in Organic Syntheses.<sup>59,60</sup>

is continued for eight hours, and the mixture is washed with water and distilled. 2,2,9,9-Tetramethyl-1,10-diphenyldecane-1,10-dione distils at 200-265°/4-8 mm. (partial decomposition); yield 70.9 g. (75%).

A suspension of 29.25 g. (0.75 mole) of sodium amide in 600 ml. of anhydrous toluene is prepared in a 2-l. flask equipped with a stirrer, a dropping funnel, and a condenser carrying a drying tube. To the toluene-sodium amide suspension is added 70.9 g. (0.19 mole) of 2,2,9,9-tetramethyl-1,10-diphenyldecane-1,10-dione. The mixture is heated under refluxing conditions with vigorous stirring for four hours and then cooled. After the gradual addition of 500 ml. of water, the mixture is filtered as rapidly as possible. The solid diamide thus obtained is washed with water, and the wash water is added to the filtrate. After the toluene is separated from the filtrate, the aqueous solution is concentrated. Upon acidification, this aqueous fraction yields a small additional amount of diamide. The total yield of crude  $\alpha,\alpha,\alpha',\alpha'$ -tetramethylsebacamide is 42 g. (87.5%). Recrystallization from ethanol results in a product melting at 210–213°.

A solution of 42 g. of erude diamide in 320 g. of concentrated sulfuric acid is cooled to 0-5° and treated with 45 g. of sodium nitrite in the minimal amount of water. The mixture is next heated to 50°, and water is added gradually with stirring. The solid acid that separates is removed by filtration, washed with water, and dissolved in aqueous sodium carbonate. The solution is decolorized with earbon, and the acid is reprecipitated with hydrochloric acid; yield 29.4 g (70%). Purification is effected by recrystallization from ethyl acetate; pure  $\alpha, \alpha, \alpha', \alpha'$ -tetramethylsebacic acid melts at 117-118°.

1-Methylcyclohexylamine Hydrochloride from Cyclohexyl Phenyl Ketone. <sup>19</sup> A suspension of 10 g. (0.25 mole) of sodium amide in 200 ml. of anhydrous toluene is prepared in a 500-ml. flask equipped with a stirrer, a dropping funnel, and a condenser carrying a drying tube. To this is added dropwise 47 g. (0.25 mole) of cyclohexyl phenyl ketone. The mixture is stirred and boiled for one hour. It is stirred and cooled in an ice bath while 71 g. (0.5 mole) of methyl iodide is added in one portion. A sudden surge of heat after five minutes causes rapid boiling of the mixture. Stirring at room temperature is continued for twenty-four hours, after which the mixture is washed with water and distilled. The 1-methylcyclohexyl phenyl ketone distils at  $134-140^{\circ}/5$  mm.,  $n_D^{25}$  1.5316; yield 42 g. (80%).

A suspension of 15.6 (0.4 mole) of sodium amide in 200 ml. of anhydrous toluene is prepared as outlined above. The toluene suspension is stirred while 42 g. (0.2 mole) of 1-methylcyclohexyl phenyl ketone is gradually added. Stirring is continued, and the mixture is heated under refluxing

conditions for six hours. After the reaction mixture is washed with water, the toluene layer is separated and distilled. 1-Methyleyelohexane-earboxamide distills at  $151-154^{\circ}/15$  mm, and crystallizes on cooling. The amide is further purified by crystallization from pentane, m.p.  $65^{\circ}$ ; yield 25 g.  $(88^{\circ})$ .

A solution of 28.8 g. (0.18 mole) of bromine in 485 ml. of 20% aqueous potassium hydroxide is stirred and cooled in an ice bath while 25 g. (0.18 mole) of 1-methyleyelohexaneearboxamide is added as a fine powder. After the mixture has been stirred for an additional one-half hour, the resulting isocyanate is extracted with ether. The ethereal extract is added dropwise with stirring to 200 ml. of boiling concentrated hydrochloric acid. After the liberation of carbon dioxide ceases, the hydrochloric acid solution is concentrated in vacuum. The crystalline residue is recrystallized from a mixture of absolute ethanol and ether. A yield of 21 g. (80%) of 1-methyleyclohexylamine hydrochloride, m.p. 285° dec., is obtained.

α,α-Dimethyl-β-phenylpropionamide from Isobutyrophenone. A suspension of 15.6 g. (0.4 mole) of sodium amide in 200 ml. of anhydrous toluene is prepared in a 500-ml. flask equipped with a stirrer, a dropping funnel, and a condenser protected by a drying tube. A solution of 60 g. (0.4 mole) of isobutyrophenone and 68.5 g. (0.4 mole) of benzyl bromide in 100 ml. of anhydrons toluene is added dropwise with stirring. The reaction mixture is heated on a steam bath for forty-eight hours and then is washed with water. The toluene solution is distilled. 2,2-Dimethyl-1,3-diphenylpropan-1-one is obtained in a 75% yield (71.4 g.), distilling at  $142-143^{\circ}/3$  mm.:  $n_{10}^{\infty}$  1.5652.

The mixture is heated and stirred for an additional hour and then cooled to room temperature, after which 21 g. (0.075 mole) of methyl iodide is added dropwise. Stirring at room temperature is continued for fifteen hours, and the benzene solution is washed with water and dried.

The dried benzene solution thus obtained is added to 6 g. (0.075 mole) of a sodium amide suspension as outlined above. The resulting sodio derivative of  $\alpha$ -methyl-n-heptyl phenyl ketone is heated in benzene under refluxing conditions, and 37 g. (0.075 mole) of n-butyl iodide is added dropwise. This mixture is heated and stirred for an additional four hours. It is cooled, washed with water, dried, and distilled. A yield of 11 g. (55%) of  $\alpha$ -n-butyl- $\alpha$ -methyl-n-heptyl phenyl ketone, b.p. 175–183°/17 mm., is obtained.

This ketone (0.04 mole) is added to a suspension of 1.6 g. (0.04 mole) of sodium amide in anhydrous benzene. The suspension is stirred and boiled for four hours and is then washed with water and distilled. A yield of 9 g. (quantitative) of  $\alpha$ -n-butyl- $\alpha$ -methylcaprylamide is distilled at  $167-169^{\circ}/18$  mm.

Without further purification, the amide so obtained is dissolved in 75 g. of concentrated sulfuric acid, and the resulting solution is excled in a freezing mixture while an excess of a cold, saturated solution of seriom nitrite is stirred in. The mixture is warmed to about 50°, diluted with water, and extracted with ether. The ethereal extract is in turn extracted with dilute sodium hydroxide solution, and the combined alkaline extracts are acidified. The α-n-butyl-α-methylcaprylic acid distils at 199-1921 18 mm.; yield 2.4 g. (28%).

ABLE I

A. Cleavage of Alexy, Aralixy, or Cycloalkyl Phenyl Ketones

References	62, 32, 63 62, 32, 15 26, 27	62, 32, 15 15, 32, 62 32, 64 28	15, 32, 62 15, 32, 62 15 86
Yield,%	Quant.	Quant.	90
Product RCONH <sub>2</sub> Formula	$\begin{array}{c} C_5 H_{11} NO \\ C_6 H_{12} NO \\ (CH_3)_2 C CH_2 \\ \downarrow \qquad \qquad \downarrow \\ O == C \\ -N \\ H \end{array}$	$\begin{array}{c} \mathrm{C_7H_3NO} \\ \mathrm{C_7H_{15}NO} \\ \mathrm{C_7H_{15}NO} \\ \mathrm{C_2H_5} \\ \mathrm{H_3CC} \mathrm{CH_2} \\ \mathrm{O} = \mathrm{C} \\ \mathrm{H} \\ \mathrm{H} \\ \mathrm{H} \end{array}$	$\begin{array}{c} C_8H_{17}NO\\ C_8H_{17}NO\\ C_8H_{17}NO\\ \end{array}$
Ketone RCOC <sub>6</sub> H <sub>5</sub> R	$(\mathrm{CH_3})_3\mathrm{C} \mathrm{C_2H_5}\mathrm{C}(\mathrm{CH_2})_2 \mathrm{CH}_2=\mathrm{CH}\mathrm{CH}_2\mathrm{C}(\mathrm{CH_3})_2-$	$n$ - $G_2^{\mu}H_2^{\mu}(GH_3)_2^{\mu}$ - $G_2^{\mu}H_3^{\mu}(GH_3)(G_2^{\mu}H_3)$ - $i$ - $G_3^{\mu}H_4^{\mu}(GH_3)_2^{\mu}$ - $GH_2^{\mu}G(GH_3)(G_2^{\mu}H_3)$ -	$(C_2H_5)_3C n.C_3H_7C(CH_3)(C_2H_5) n.C_4H_9C(CH_3)_2 C(CH_3)_2-$

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References 63 15 15 16 15 32, 75 32, 75	32, 75 70, 25, 71, 72 70, 72, 32, 75 83 83 83 83 83 83	15 15 15 68 15, 65, 66
Yield, %	ca. 40 90, 83 ca. 90 1	Quant.
Product RCONH <sub>2</sub> Formula C <sub>11</sub> H <sub>22</sub> NO C <sub>11</sub> H <sub>22</sub> NO C <sub>11</sub> H <sub>22</sub> NO C <sub>11</sub> H <sub>22</sub> NO† C <sub>11</sub> H <sub>22</sub> NO† C <sub>11</sub> H <sub>22</sub> NO† C <sub>12</sub> H <sub>17</sub> NO C <sub>12</sub> H <sub>17</sub> NO	C <sub>12</sub> H <sub>17</sub> NO C <sub>12</sub> H <sub>17</sub> NO C <sub>12</sub> H <sub>17</sub> NO§ C <sub>12</sub> H <sub>17</sub> NO <sub>2</sub> C <sub>12</sub> H <sub>27</sub> NO C <sub>12</sub> H <sub>23</sub> NO C <sub>12</sub> H <sub>23</sub> NO C(CH <sub>3</sub> ) <sub>2</sub> CONH <sub>2</sub>	\C(CH <sub>3</sub> ) <sub>2</sub> CONH <sub>2</sub> C <sub>12</sub> H <sub>25</sub> NO† C <sub>12</sub> H <sub>25</sub> NO† C <sub>12</sub> H <sub>25</sub> NO C <sub>12</sub> H <sub>25</sub> NO C <sub>12</sub> H <sub>25</sub> NO
Ketone RCOG,H <sub>5</sub> R n-C,H <sub>15</sub> C(CH <sub>3</sub> ) <sub>2</sub> — CH <sub>3</sub> C(C <sub>4</sub> H <sub>9</sub> ·n) <sub>2</sub> — n-C,H <sub>9</sub> C(C <sub>2</sub> H <sub>5</sub> )(C <sub>3</sub> H <sub>7</sub> ·n)— n-C,H <sub>13</sub> C(C <sub>2</sub> H <sub>5</sub> )(C <sub>2</sub> H <sub>5</sub> )— c <sub>4</sub> H <sub>13</sub> C(CH <sub>3</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — n-C <sub>6</sub> H <sub>13</sub> C(CH <sub>3</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> —	o.CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — m.CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — p.CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>5</sub> C(CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — m.CH <sub>3</sub> C <sub>6</sub> H <sub>1</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>3</sub> C(CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>1</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>1</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>1</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>1</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — c <sub>6</sub> H <sub>1</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> —	$n.C_5H_{11}C(C_2H_5)(C_3H_7\cdot n) n.C_6H_{13}C(C_2H_5)_2 n.C_6H_{13}C(CH_3)(C_4H_9\cdot n) n.C_4H_9CH(C_2H_5)CH_2$

CH2C(CH3)2—	$\mathrm{C_{13}H_{15}NOS}$	1	80	
C.H.;(CH.),C(CH.),—	$c_{13}H_{19}NO$	1 8	69	
$C_6H_5CH_2C(C_2H_5)_2^{}$	$c_{13}H_{19}NO$	Cg. : 20	25	01
$C_6H_5CH_2C(CH_3)(C_3H_7\cdot n)$ —	C <sub>13</sub> H <sub>19</sub> NO <sub>3</sub>	1	77	
$C_0H_5CH(C_2H_5)C(CH_3)_2$ —	C <sub>13</sub> H <sub>19</sub> NO 3	76	78	~ ' -
$p$ -CH $_3$ OC $_0$ H $_4$ (CH $_2$ ) $_2$ C(CH $_3$ ) $_2$ —	Clarification of the NO	1	83	
$m$ -CH $_3$ C $_6$ H $_{10}$ (CH $_2$ ) $_2$ C(CH $_3$ ) $_2$ — C $_6$ H $_5$ COC(CH $_3$ ) $_6$ (CH $_3$ ) $_5$ (CH $_3$ ) $_2$ —	$\sim 13^{+2}$ $\sim 13^{+2}$ $\sim 13^{+2}$ $\sim 13^{-1}$ $\sim 13$	87*	53	- 01
	(ĆH <sub>2</sub> ) <sub>5</sub>			
	C(Cha)2COMA22	1	15	,_,
$n \cdot C_5H_{11}C(C_2H_5)(C_4H_9 \cdot n) - C_5H_{11}C(C_2H_5)$	Clarify O+	1	15	
$n \cdot \mathrm{C}_{\mathrm{cH}_{13}\mathrm{C}(\mathrm{C}_{2}^{2}\mathrm{H}_{5})(\mathrm{C}_{3}\mathrm{H}_{7}\cdot n)} -$	013112710 0+ 01-H-N0	*46	15	
n-C <sub>7</sub> H <sub>18</sub> C(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> — n-C <sub>7</sub> H <sub>1</sub> C(C <sub>1</sub> H <sub>2</sub> )	CraHorNO	7.1	99	
(CH3) C(CH3) ——(CH3) ——	$c_{14}^{13}E_{17}^{21}$	***************************************	80	
8/8				
CH2 C(CH3)2—	$C_{14}H_{19}NO$	1	79	
C, H. CH. C/C, H. 1/C, Hn)	C,H.NO8	***************************************	25, 71	
$CH_2 = C(CH_3)(CH_2)_3 C(CH_3)(CH_2)_2 C(CH_3)_2 $	$C_{14}H_{27}^{-1}NO$	1	66, 67	-~
Note: References 62-96 are listed on p. 36. * This was the yield of crude product. † Represented was else isolated				
+ the second was also isolated.				

† The principal product was benzamide. § The hydrocarbon RH corresponding to the R group in the ketone was also isolated.

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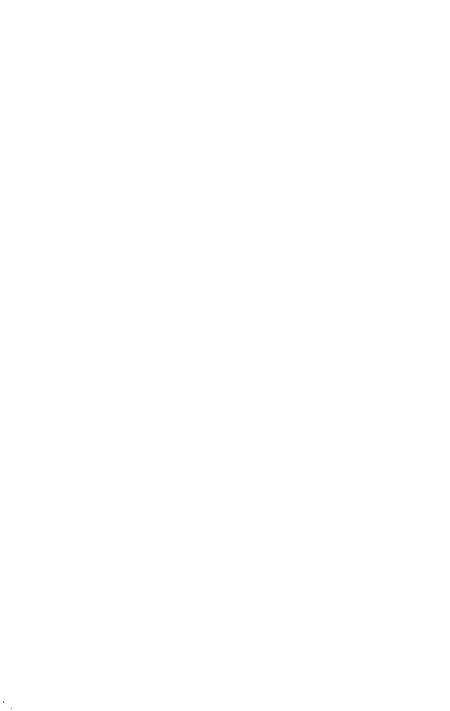
		ORO	ANIC RE	EACTIO	ONS	
References 23	15	30, 32, 64, 65 82 85	88	76, 77 70, 72	66, 67 23	15 15 65 65 82 85
Yiold,% 87		**	I	)     00:   00:	59 39*	Low
Product RCONH <sub>2</sub> Rormula	C(CE <sub>3</sub> ) <sub>2</sub> COM <sub>2</sub> (CH <sub>2</sub> ) <sub>6</sub> C(CE <sub>3</sub> ) <sub>2</sub> CONH <sub>2</sub>	$C_{14}\mathrm{H}_{29}\mathrm{NO}_{7}^{+}$ $C_{14}\mathrm{H}_{29}\mathrm{NO}$ $C_{15}\mathrm{H}_{17}\mathrm{NO}$	$C_{1_5}H_{17}N0 \\ C(CH_3)CH_2C_6H_5\S \\ C \\ C \\ C$	Grena Note	$C_{15}H_{23}NO$ . $C_{15}H_{29}NO$ . $C_{15}H_{29}NO$ . $C(CH_3)_2CONH_2$ . $(CH_2)_7$ . $CONH_2$	C <sub>15</sub> H <sub>21</sub> NO† C <sub>15</sub> H <sub>31</sub> NO† C <sub>15</sub> H <sub>31</sub> NO C <sub>15</sub> H <sub>31</sub> NO C <sub>16</sub> H <sub>19</sub> NO C <sub>16</sub> H <sub>19</sub> NO
$\begin{array}{c} {\rm Kotone} \ {\rm RCOC_6H_5} \\ {\rm R} \end{array}$	$\mathrm{C_6H_5COC(CH_3)_2(CH_2)_6C(CH_3)_2}$ —	$n.C_0H_{13}C(C_2H_5)(C_1H_9\cdot n)-n.C_1_0H_{21}C(CH_3)_2-n.C_1_0H_{2$	β·G <sub>1</sub> O <sub>1</sub> CH <sub>2</sub> O(CH <sub>3</sub> )2— [==]C(CH <sub>3</sub> )(C <sub>6</sub> H <sub>6</sub> CH <sub>2</sub> )—	$C_{H,CH(C,H_{1})}C(C_{2}H_{5})_{2}$	p.(CH <sub>3</sub> ) <sub>3</sub> CC <sub>6</sub> H <sub>3</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> — CH <sub>2</sub> =CH(CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>3</sub> ) <sub>2</sub> — C <sub>6</sub> H <sub>5</sub> COC(CH <sub>3</sub> ) <sub>2</sub> (CH <sub>2</sub> ) <sub>7</sub> C(CH <sub>3</sub> ) <sub>2</sub> —	$n.C_6H_{13}C(C_2H_5)(C_5H_{11}.n) n.C_9H_{15}C(C_2H_5)(C_4H_9.n) n.C_1H_{15}C(C_2H_5)(C_4H_9.n) n.C_1H_{23}C(CH_3)(C_2H_5) a.C_1H_{23}C(CH_3)^2 a.C_1OH_{23}C(CH_3)^2 \beta.C_1OH_{23}C(CH_3)(C_2H_5)-$

CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> —	$C_{16}H_{19}NO$	50	85
$\begin{array}{c c} & & & & \\ & \sim C_{10} H_7(\mathrm{CH}_2)_2 \mathrm{C}(\mathrm{CH}_3)_2 \\ & \sim C_6 H_5 \mathrm{COC}(\mathrm{CH}_3)_2 \mathrm{CH}_2 \mathrm{C}_6 H_4 \mathrm{CH}_2 \mathrm{C}(\mathrm{CH}_3)_2 \end{array}$	$\mathrm{C_{16}H_{19}NO}_{\mathrm{CC}_{2}\mathrm{C}(\mathrm{CH}_{3})_{2}\mathrm{CONH}_{2}}$	08	81, 82 25
$m$ ·C $_6\mathrm{H}_5\mathrm{COC}(\mathrm{CH}_3)_2\mathrm{CH}_2\mathrm{C}_6\mathrm{H}_4\mathrm{CH}_2\mathrm{C}(\mathrm{CH}_3)_2$ —	$^{\prime}$	Į	25
$p\text{-}\mathrm{c}_{_{\mathbf{i}}}\mathrm{H}_{_{\mathbf{j}}}\mathrm{COC}(\mathrm{CH}_{_{3}})_{_{2}}\mathrm{CH}_{_{2}}\mathrm{C}_{_{\mathbf{i}}}\mathrm{H}_{_{4}}\mathrm{CH}_{_{2}}\mathrm{C}(\mathrm{CH}_{3})_{_{2}}$	$\begin{array}{c} \text{CH}_2\text{C}(\text{CH}_3)_2\text{CONH}_2\\ \text{CH}_2\text{C}(\text{CH}_3)_2\text{CONH}_2\\ \end{array}$	I	25
$\mathrm{C_6H_5COC(CH_{3)_2(CH_2)_8C(CH_3)_2}-}$	$^{ackslash_2}$ C(CH $_3$ ) $_2$ CONH $_2$ (CH $_2$ ) $_3$ CONH $_2$	50 *	23
$n\cdot \mathrm{C_8H_{17}C(C_2H_5)(C_4H_0-n)}$ —	$\sim$ C(CH <sub>3</sub> ) $_2$ CONH $_2$	Low	15

Note: References 62-96 are listed on p. 36.

\* This was the yield of crude product.

† Benzamide was also isolated. ‡ The principal product was benzamide. § The hydrocarbon RH corresponding to the R group in the ketone was also isolated. || The product was isolated as the acid.



${ m C_6H_5COC(CH_3)_2(CH_2)_{10}C(CH_3)_2}$ —	$C(CH_3)_2CONH_2$	*98	53
	$\langle C(CH_3)_2CONH_2 \ C_{n,H_1,n}NO_1$	I	15
$n$ -C <sub>10</sub> +121 $<$ ( $<_2$ +15/ $<_4$ +19 $<$ ) $<_7$ -C <sub>1</sub> +1. $<$ (CH <sub>3</sub> ),	C <sub>18</sub> H <sub>37</sub> NO	Quant.	89
$(H_2^{-2})(C_2^{-1})$ $(H_2^{-2}(CH_3)(C_2^{-1}H_5) - (C_2^{-1}H_3)$	$C_{20}H_{27}NO$	1	83
$(\mathrm{CH}_2)_{\mathrm{II}}\mathrm{C}(\mathrm{CH}_3)_{\mathrm{2}}$	$\mathrm{C_{20}H_{37}NO}$	Quant.	87
$n ext{-} ext{C}_{1_6 ext{H}_{33} ext{C}( ext{CH}_3)_2 ext{-}}$	$\mathrm{C_{20}H_{11}NO}$	i	30, 68
(CH <sub>2</sub> ) <sub>13</sub> C(CH <sub>3</sub> ) <sub>2</sub> —	$\mathrm{C_{21}H_{39}NO}$	1	89
CH <sub>3</sub> (CH <sub>2</sub> ),CH=CH(CH <sub>2</sub> ) <sub>8</sub> C(CH <sub>3</sub> ) <sub>2</sub> —	$\mathrm{C}_{22}\mathrm{H}_{43}\mathrm{NO}$	ı	89
$C_6H_5COC(CH_3)_2(CH_2)_{14}C(CH_3)_2$ —	$\sim$ C(CH <sub>3</sub> ) <sub>2</sub> CONH <sub>2</sub> (CH <sub>2</sub> ) <sub>14</sub>	I	<del>1</del> 61
	C(CH <sub>3</sub> ),CONH,		
$n \cdot C_{18}H_{37}C(CH_3)_2$ —	$C_{22}H_{45}NO$	I	65
$n\text{-}\mathrm{C}_{12}\mathrm{H}_{25}\mathrm{C}(\mathrm{C}_{2}\mathrm{H}_{5})(\mathrm{C}_{10}\mathrm{H}_{21}\text{-}n)$ —	$c_{2_6H_{53}NO\dagger}$	$  \mathbf{Low}  $	15
$_{\mathrm{CH_2}\text{-CHCH_2C(CH_3)_2}}^{\mathrm{CH_2}\text{-CHCH_2C(CH_3)_2}}$	No reaction	I	G G
Note: References 62-96 are listed on p. 36.			

\* The principal product was benzamide.

§ The hydrocarbon RH corresponding to the R group in the ketone was also isolated.

| The product was isolated as the acid. \* This was the yield of crude product. † Benzamide was also isolated.

TABLE 1 (Part B)—Continued

Ketone RCOC <sub>6</sub> H <sub>5</sub>	Product RCONH <sub>2</sub>		
R	Formula	Yield, %	Reference
CH <sub>2</sub> —CH <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	$C_9H_{17}NO$	65	19
CH <sub>2</sub> —CH <sub>2</sub>			
CH <sub>2</sub> —CHCH <sub>3</sub> C <sub>3</sub> H <sub>7</sub> ·n	C <sub>10</sub> H <sub>19</sub> NO	weekee	18
CH <sub>2</sub> —CH <sub>2</sub>			
CH_CH <sub>2</sub> CH <sub>3</sub>	$C_{10}H_{10}NO$		89
$^{\mid}_{\mathrm{C_3H_7-}i}$			
	Н <sub>3</sub> С <sub>10</sub> Н <sub>19</sub> NО	68	90
$\mathrm{CH_2-CH_2}$ $\mathrm{C_3H_7}$ - $n$ $\mathrm{CH_2-CH_2}$	$\mathrm{C_{10}H_{19}NO}$	65	19
$\begin{array}{c} \operatorname{CH}_2 \\   \\ \operatorname{CH}_2 \end{array} \subset \begin{array}{c} \operatorname{CH}_2 \operatorname{C}_6 \operatorname{H}_5 \\ \end{array}$	$\mathrm{C_{11}H_{13}NO}$	56	20, 17
$CH_2$ — $CH_2$ $C_4H_9$ - $n$	$\mathrm{C_{11}H_{21}NO}$	66	19
$\begin{array}{c} \mathrm{CH_2-CH_2} \\ \mathrm{C_6H_5} \\ \mathrm{CH_2} \\ \mathrm{CH_2-CH_2} \end{array}$	C <sub>12</sub> H <sub>13</sub> NO*†		44

Note: References 62-96 are listed on p. 36.

\* Benzamide was also isolated.

\* Benzamide was also isolated.
† The hydrocarbon RH corresponding to the R group in the ketone was also isolated.



# TABLE II

CLEAVAGE OF ALIPHATIC KETONES

	À			
Ketone RCOK'	Κ'		i i	References
PŽ	ዄ፞	Formula	Products	Treferences
		C,H,0	$(CH_3)_3CCONH_2$ , $(CH_3)_3CH$	91
(CH <sub>3</sub> ) <sub>3</sub> C—	$C_2H_5C(CH_3)_2$	$C_{10}H_{20}O$	. D	32, 91
		1		29 01
C.H.C(CH.),—	C,H,C(CH,3),—	$\mathrm{c_{11}H_{22}O}$	$C_2H_5C(CH_3)_2CUNH_2$ , $C_2H_5CH(CH_3)_2$	0.00 U
2/62-8-2-1 -J CHJ)	(C, H, ), C,	C,H,D	$(CH_3)_3CCONH_2$ , $(C_2H_5)_3CCONH_2$	32, 91
(0113/30	5,6 -15 -1	3	(ratio 5:1); (CH <sub>3</sub> ) <sub>3</sub> CH, (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> CH	
(CH2),CHC(CH3),—	(CH,),CHC(CH,),— C <sub>13</sub> H <sub>26</sub> O	$C_{l,3}H_{26}O$	Z	32
(CH <sub>2</sub> ), C—	C,H,CH,C(CH,), C <sub>15</sub> H,20	$C_{15}H_{22}O$	$(CH_3)_3CCONH_2$ , $C_6H_5CH_2CH(CH_3)_2$	32
(CH <sub>3</sub> ),C—	$C_{17}^{'}E_{12}^{'}CC_{2}^{'}E_{13}^{'}CC_{2}^{'}E_{13}^{'}CC_{17}^{'}E_{26}^{'}CC_{17}^{'$	$c_{17}^{ m H}_{26}^{ m O}$		32
			$\mathrm{C_6H_5CH_2CH(C_2H_5)_2}$	
$C_6H_5C(\mathrm{CH_3})_2$ —	$C_6H_5C(CH_3)_2$ —	$\mathrm{C}_{21}\mathrm{H}_{26}\mathrm{O}$	$c_{21}H_{26}O = c_6H_5C(CH_3)_2CONH_2$ , $c_6H_5CH(CH_3)_2$	32

Note: References 62-96 are listed on p. 36.

# ABLE III

# EAVAGE OF AROMATIC KETONES

	References	6	∞	<b>∞</b>	δ	ø	5, 8, 36	11	5, 36	8, 9, 11	11	11	11, 5, 8,	34	34	34
CLEAVAGE OF AROMATIC KETONES	Products	$C_6H_5CONH_2$ , 2. $C_4H_3SCONH_2$ (ratio 2.5 : 1 as acids)	$C_6H_5CONH_2$ , 3-Br $C_6H_4CONH_2$ (ratio 5.5 : 1 as acids)	C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub> , 4·BrC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> (ratio 2.5: 1 as acids)	$C_6H_5CONH_2$ , 3-CIC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> (ratio 11 : 1 as acids)	$C_6H_5CONH_2$ , 4-CIC $_6H_4CONH_2$ (ratio 3.2 : 1 as acids)	$C_6H_5CONH_2$	No cleavage*	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> , C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub> (slightly more of former)	C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub> , 4-CH <sub>3</sub> SC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub> (poor yield)	$C_6H_5CONH_2$ , 3- $CH_3OC_6H_4CONH_2$ (ratio 3.6 : 1 as acids)	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> , C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub> (ratio 2.5 · 1 as acids)	2,4-(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CONH <sub>2</sub> , C <sub>c</sub> H <sub>c</sub> CONH <sub>2</sub> (mainly the latter)	2,5-(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>2</sub> CONH <sub>2</sub> , C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub> (mainly the latter)†	3,4-(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CONH <sub>2</sub> , C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub> (equal amounts)
CLEAVAGE OF A	Formula	$c_{11}H_{8}os$	$\mathrm{C}_{13}\mathrm{H}_{9}\mathrm{BrO}$	$\mathrm{C_{13}H_9BrO}$	$C_{13}\mathrm{H}_9\mathrm{ClO}$	$C_{13}H_9ClO$	$\mathrm{C_{13}H_{10}O}$	$\mathrm{C_{14}H_9NO}$	$\mathrm{C}_{\mathrm{I}_4}\mathrm{H}_{\mathrm{12}}\mathrm{O}$	$\mathrm{C_{14}H_{12}OS}$	$\mathrm{C_{14}H_{12}O_2}$	$\mathrm{C_{14}H_{12}O_{2}}$	$\mathrm{C}_{14}\mathrm{H}_{12}\mathrm{O}_2$	$\mathrm{C_{15}H_{14}O}$	$\mathrm{C}_{15}\mathrm{H}_{14}\mathrm{O}$	$\mathrm{C_{15}H_{14}O}$
	Kotone ArCOAr' Ar'	$2 \cdot \mathrm{C_4H_3S}$	$3 ext{-BrC}_6 H_4$ —	$^{4} ext{-BrC}_{6} ext{H}_{4} ext{}$	$3$ -CIC $_6$ H $_4$ —	$4\cdot \mathrm{CIC}_6\mathrm{H}_4$ —	$C_6H_6$ —	$^{4}$ -CNC $_{6}$ H $_{4}$ —	$^{4} ext{-CH}_{3} ext{C}_{6} ext{H}_{4} ext{}$	$_4$ -CH $_3$ SC $_6$ H $_4$ —	$2\text{-CH}_3\text{OC}_6\text{H}_4$	$3$ -CH $_3$ OC $_6$ H $_4$ —	$_4$ -CH $_3$ OC $_6$ H $_4$ —	$2,4$ -(CH $_3$ ) $_2$ C $_6$ H $_3$ —	$2,5\cdot({ m CH_3})_2{ m C_6H_3}$	$3,4\cdot({\rm CH_3})_2{\rm C_6H_3}-$
	Ar	$C_6H_5-$	$C_6H_5-$	$C_6H_5$ —	$C_6H_5$	$C_6H_5$ —	$c_{_6\mathrm{H_5}}$	$C_{\mathbf{f}}H_{\mathbf{f}}$	$c_{ m eH_5}$	$C_6H_5$	C <sub>6</sub> H <sub>5</sub> —	C <sub>6</sub> H <sub>5</sub> —	$c_{ m eH_{ m i}}$	$C_6H_5$	$C_{ m c}H_{ m 2}$	$C_6H_5-$

11	11	11	∞ :	11	11	34	9, 34	33	9, 33	33	33	33	33	σ	
4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> , 3-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub> tratio 6.3 : 1 as acids)	CoHo (poor yield)	$C_6H_5CONH_2$ (poor yield) $C_6H_5CONH_2$ , 3,4-(CH <sub>3</sub> O) $_2C_6H_3CONH_2$	C <sub>6</sub> H <sub>5</sub> CONH <sub>2</sub> , 4-(CH <sub>3</sub> ) <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub>	$3,4\cdot(\mathrm{CH_3O})_2\mathrm{C_6H_3CONH_2}$ $3\cdot\mathrm{CH_3OC_6H_4CONH_2}$	3.4.(CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CONH <sub>2</sub> 4.CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CONH <sub>2</sub>	C,H,CONH,, C,nH, (trace)	2-C <sub>10</sub> H <sub>2</sub> CONH <sub>2</sub> , $C_6H_5$ CONH <sub>2</sub> (ratio 6 : 1); (ratio 2 : 1 as acids)	$4 \cdot C_6 H_5 C_6 H_4 CONH_2$ , $4 \cdot CIC_6 H_4 CONH_2$ (ratio 2.3 : 1 as acids)	$C_6H_5 CONH_2$ , $4 \cdot C_6H_5 C_6H_4 CONH_2$ (ratio 3 : 1 as acids)	$4 \cdot C_0 H_5 C_0 H_4 CONH_2$ , $4 \cdot CH_3 C_0 H_4 CONH_2$ (ratio 1.08 : 1 as acids)	$4 \cdot C_0 H_5 C_6 H_4 CONH_2$ , $4 \cdot CH_3 OC_6 H_4 CONH_2$ (ratio 1.45 : 1 as acids)	$^{4-{ m C}_{ m c}}_{ m H_5{ m C}_{ m c}{ m H_4}{ m CONH}_2}$ , ${ m C}_{ m 10}{ m H}_{ m g}$ (10% of	$4 \cdot C_0 H_5 C_0 H_1 CONH_2$ , $2 \cdot C_1 OH_7 CONH_2$	No reaction	
$C_{15}H_{14}O_{3}$	$\mathrm{C_{15}H_{14}O_{3}}$	$c_{15}^{ m H_{14}}O_3^{ m C}$	$c_{15}H_{15}NO$	$\mathrm{C_{16}H_{16}O_{4}}$	$\mathrm{C_{16}H_{16}O_{4}}$	C,,H,,O	$c_{1}^{'}H_{12}^{'}0$	$\mathrm{C}_{19}\mathrm{H}_{13}\mathrm{ClO}$	$\mathrm{C_{19}H_{14}O}$	$\mathrm{C_{20}H_{16}O}$	$\mathrm{C_{20}H_{16}O_{2}}$	$\mathrm{C_{23}H_{16}O}$	$c_{23}H_{16}O$	$\mathrm{C_{26}H_{20}O}$	
$3\text{-CH}_3\text{OC}_6\text{H}_4$	$_{2,4\text{-}(\mathrm{CH}_{3}\mathrm{O})_{2}\mathrm{C}_{6}\mathrm{H}_{3}}$	$2,5-(\mathrm{CH_3O})_2^2\mathrm{C}_6^6\mathrm{H_3}-3,4-(\mathrm{CH_3O})_2^2\mathrm{C}_6^6\mathrm{H_3}-$	4-(CH <sub>3</sub> ) <sub>9</sub> NC <sub>6</sub> H <sub>3</sub> —	3,4-(CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> —	3,4-(CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> —	H. J.1	2-C <sub>10</sub> H,—	$_{ m 4^{ ext{-}}C_6H_5C_6H_4^{ ext{}}}$	$_4$ . $_{\mathrm{C_6H_5C_6H_4}}$	$^4$ -C $_6$ H $_5$ C $_6$ H $_4$ —	$_4$ - $_6$ H $_6$ C $_6$ H $_4$ —	$_4$ - $_6$ H $_5$ C $_6$ H $_4$ —	$+C_6H_5C_6H_4$	$H_5$ — $(C_6H_5)_3C$ — Note: References 62–96 are listed on p. 36.	
$4$ -CH $_3$ OC $_6$ H $_4$ —	C.H.,—	С. С. С. В.	î H.O	$3.\mathrm{CH_3OC_6H_4}$	$4$ -CH $_3$ OC $_6$ H $_4$ —	þ	C <sub>6</sub> H <sub>5</sub> -	$4.\mathrm{CIC_6H_4}$	$C_6H_5$ —	$^4$ -CH $_3$ C $_6$ H $_4$ —	$4 \cdot \mathrm{CH_3OC_6H_4}$	$^{1\cdot C_{10}H_7-}$	$2 ext{-C}_{10} ext{H}_{7}$	C <sub>6</sub> H <sub>5</sub> — <i>Note:</i> Reference:	# Tr. +line course

\* In this experiment the evano group was hydrolyzed and the product was  $p.C_6H_5COC_6H_4CO_2H$ † Catalytic quantities of mercury were added in a second experiment; 2,5-dimethylbenzamide and benzamide were obtained in a ratio of 1:3.5.

TABLE IV

CLEAVAGE OF ALICYCLIC KETONES

References 92 39  $C_{10}H_{19}NO$  $C_9H_{19}NO$ Formula  $C_9H_{17}NO$  $(CH_3)_2CH(CH_2)_2C(CH_3)_2CONH_2$ CONH CONH Products Ketone

 $C_{11}H_{15}NO$  $\mathrm{C}_{10}\mathrm{H}_{21}\mathrm{NO}$ (CH<sub>3</sub>),CHCH(CH<sub>3</sub>)CH<sub>2</sub>C(CH<sub>3</sub>),CONH<sub>2</sub> and (CH<sub>3</sub>),CHCH<sub>2</sub>CH<sub>3</sub>CONH<sub>2</sub> C6H5CH2C(CH3)2CONH2

-CH3

73, 74, 88

96

TABLE IV (Continued)

CLEAVAGE OF ALICYCLIC KETONES

		ORG	MINIO ME	101101113			
Referenco	93	38		93	38		92
Formula	$\mathrm{C_{16}H_{33}NO}$	$\mathrm{C_{10}H_{20}NO}$		$\mathrm{C_{21}H_{29}NO}$	$c_{21}H_{31}N0$		
CLEAVAGE OF ALICYCLIC INSTONES  Products	$_{\mathrm{C}_{\mathrm{a}}}$ H,CH(CH $_{\mathrm{a}}$ )CH $_{\mathrm{c}}$ CH(CH $_{\mathrm{a}}$ )C(C $_{\mathrm{a}}$ H $_{\mathrm{a}}$ ) $_{\mathrm{a}}$ CONH $_{\mathrm{a}}$ and	$(c_3H_7)_2$ CHCH $(CH_3)$ CH $_2$ C(CH $_3$ ) $(c_3H_7)$ CONH $_2$ CH $_3$ CH	$C_6H_5CH_2(C_2H_5)HC$ $(CH_5)_2$	$C_6H_5$ CH(CH <sub>3</sub> )CH <sub>2</sub> CH(CH <sub>3</sub> )C(CH <sub>3</sub> )(CH <sub>3</sub> C <sub>6</sub> H <sub>5</sub> )CONH <sub>2</sub>	and C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CH(CH <sub>3</sub> )CH <sub>2</sub> C(CL <sub>3</sub> )CL <sub>2</sub> C <sub>7</sub> C <sub>5</sub> C <sub>7</sub>	$(C_6H_5CH_2)_2HC$ (CH <sub>3</sub> ) <sub>2</sub>	No reaction
Ketone		C.H.	Y"	CH <sub>3</sub> CH <sub>3</sub> CH <sub>3</sub>	$CH_2$ $CH_2C_6H_5$ $CH_2C_6H_5$ )2	0=	сн., (Сн.),

### REFERENCES

- 42 Haffer and Baner, Compt. rend., 148, 127 (1909).
- 69 Grunfeld, Ann. chim. Parls, [10] 20, 301 (1933).
- 44 Hafter and Bauer, Champt, rend., 149, 5 (1909).
- 45 Mentyor, Bun Hol, and Cagniant, Bull, soc, chim. France, [5] 10, 141 (1943).
- at Bon Mid and Cogninal, Hee, trav. chim., 65, 248 (1946).
- 57 Laboratolu s françois de chimiethérajée, Brit. pat. 617,892 (1949) [C. A., 43, 7037 (1919)].
- <sup>88</sup> Ban Hal and Cagabart, Z. physiol. Chem., 279, 76 (1943).
- \*\* Humart and Hach, Hall, soc, china, France, [5] 5, 238 (1938).
- 20 Montger, Ban Moi, and Capalant, Bull. soc, chlm. France, (5) 0, 813 (1912).
- <sup>21</sup> Buller and Damesall, Compt. rend., 153, 111 (1911).
- <sup>22</sup> Lubenateires Trançais do chimiothérapie, Brit. pat. 613,111 [O. A., 43, 5800 (1919)].
- 78 Haller and Bauer, Compt. rend., 150, 1472 (1910).
- <sup>76</sup> Haller and Bauer, Ann. chim. Paris, [9] 19, 340 (1921).
- <sup>76</sup> Haller and Bauer, Compt. rend., 153, 21 (1911).
- 26 Hamart, Albesea, and Haller, Compt. rend., 174, 1289 (1922).
- <sup>27</sup> Alberen, Ann. chim. Paris, [9] 18, 216 (1922).
- 78 Burolloi and Capaiant, Compt. rend., 219, 455 (1914).
- 29 Cagainat, Compt. rend., 226, 675 (1948).
- \*9 Cogniant, Hull, soc. chim. France, 1949, 382 (5-6).
- \*) Inducatoires Irançais de éldinfothéraple, llwise par. 238,798 (1945).
- \*2 Cagainat, Mentver, and Buttillot, Bull. soc. ckim. France, [5] 10, 146 (1919).
- 83 Mentzer and Chemin, Bull. soc. chim, France, [5] 15, 586 (1948).
- \*\* Mentzer, Ban-Hol, and Cagaiant, Rwles pat. 237,879 (1945).
- \*5 Cognitud and Ban-Hol, Hall, soc, chlin, France, [5] 10, 349 (1943).
- 86 Burr Hed and Chyalant, Garapt, rend., 237, 26 (1943).
- 87 Bun-Hol and Cagainat, Bull, soc, chim. France, [5] B, 355 (1012).
- \*\* Bothstein and Saville, J. Olem. Hon., 1949, 1946.
- 44 Bouvewitt and Levisticis, Hull. noc. chim. France, [4] B, 968 (1919).
- 40 Blive, Borevzy, and Lachte, J. Am, Okem, Rac., 62, 2744 (1940).
- (1) Huller and Bauer, Compt. revol., 150, 664 (1910).
- \*2 Tannetkin and Yagan, J. Gen. Chem. U.S.St. R., 10, 885 (1940) [C. A., 41, 2019 (1947)].
- 48 Haller and Cornubert, Compt. rend., 158, 1739 (1914).
- 94 Hollor and Ramart-Lucas, Compt. rend., 173, 682 (1921).
- \*\* Buller and Bauer, Ann. chim. Paris, [9] 8, 117 (1917).
- <sup>95</sup> Haller and Carnabert, Omept. rend., 158, 1610 (1914).

# CHAPTER 2

# THE GATTERMANN SYNTHESIS OF ALDEHYDES

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ojo-zamernj ipj 110ie-z-em vozamenjao · · · · · · · · · · · · · · · · · · ·	57

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### INTRODUCTION

Gattermann developed two methods for introducing the aldehyde group into aromatic compounds. The first of these, known as the Gattermann-Koch reaction, uses a mixture of earbon monoxide and hydrogen chloride in the presence of a mixture of anhydrous aluminum chloride and cuprous chloride. It is not adaptable to the preparation of aldehydes

$$ArH + CO + HCl \xrightarrow{AlCl_2} ArCHO + HCl$$

from phenols or phenolic others, however. The second method employs a mixture of hydrogen eyanide and hydrogen ehloride with or without a catalyst, and permits the introduction of an aldehyde group into phenols, naphthols, and their ethers, and, under special conditions, into aromatic hydrocarbons and related compounds.2 This chapter is concerned with the second method.

$$ArH + HCN + HCl \xrightarrow{(1) AlCl_3 \text{ or } ZnCl_2} ArCHO + NH_4Cl$$

Aluminum chloride must be used as a catalyst with certain phenols and phenolic ethers;3 with others, zinc chloride may replace aluminum chloride.4 A modification of this method, which was described by Adams and his co-workers, 5,6 employs zinc cyanide as both a convenient source of anhydrous hydrogen cyanide and as a catalyst. When hydrogen chloride is introduced into the reaction mixture, hydrogen cyanide and zinc chloride are formed in situ. In those reactions that require anhydrous aluminum chloride as a catalyst, it may be introduced with the zinc cyanide. Polyhydric phenols such as resorcinol and phloroglucinol in which the hydroxyl groups are meta to each other do not require a catalyst.3

More vigorous conditions are required to introduce the aldchyde group into aromatic hydrocarbons; e.g., the temperature must be raised. 7,8

<sup>1</sup> Crounse, Organic Reactions, 5, 290, John Wiley & Sons, 1949.

<sup>&</sup>lt;sup>2</sup> Gattermann, Ber., 31, 1149 (1898). <sup>3</sup> Gattermann, Ann., 357, 313 (1907).

<sup>&</sup>lt;sup>4</sup> Gattermann and von Horlacher, Ber., 32, 284 (1899). <sup>5</sup> Adams and Levine, J. Am. Chem. Soc., 45, 2373 (1923).

<sup>&</sup>lt;sup>6</sup> Adams and Montgomery, J. Am. Chem. Soc., 46, 1518 (1924).

<sup>&</sup>lt;sup>7</sup> Hinkel, Ayling, and Beynon, J. Chem. Soc., 1936, 339. 8 Hinkel, Ayling, and Morgan, J. Chem. Soc., 1932, 2793.

The choice of solvent and the proportion of aluminum chloride and hydrogen eyanide relative to the amount of hydrocarbon present affect the yields obtained. Zine eyanide or sodium eyanide may be used in place of hydrogen eyanide.<sup>8,9</sup>

### MECHANISM

The mechanism of the reaction appears to be complex and has not been fully chicidated. Hinkel and his co-workers have presented evidence indicating that the mechanism may vary with the nature of the compound into which the aldehyde group is being introduced and with the conditions of reaction.<sup>8,10-14</sup> A study has been made of the products of the reaction of hydrogen cyanide, hydrogen chloride, and aluminum chloride with each other in the absence of an aromatic nucleus in order to find one or more species which might be serving as the agent of aromatic substitution. Thus, hydrogen cyanide reacts with aluminum chloride to give a complex with the structure I,<sup>13</sup> and with hydrogen chloride to give the "sesquichloride" II.<sup>15,16</sup> In turn, II gives chloromethyleneformamidine (III) when heated to 100°,<sup>12</sup> and iminoformylearbylamine (IV) when heated with quinoline.<sup>17</sup> Aluminum chloride complexes of these latter substances

were also prepared.<sup>10,12,13</sup> Since modern spectral methods were unavailable at the time this work was carried out, and in view of the experimental difficulties involved in characterizing such compounds, further investigation is desirable before the structures assigned can be considered as definitely established.

Although one or more of the substances mentioned or ions derived from them may serve as intermediates in the Gattermann reaction, it should be noted that yields of aldehydes in excess of 50% based on the hydrogen cyanide employed are often obtained. It follows then that, if an intermediate such as I, II, III, or IV is effective as the aromatic substituting

<sup>&</sup>lt;sup>9</sup> Niedzielski and Nord, J. Am. Chem. Soc., 63, 1462 (1941).

<sup>&</sup>lt;sup>10</sup> Hinkel, Ayling, and Beynon, J. Chem. Soc., 1935, 674.

<sup>&</sup>lt;sup>11</sup> Hinkel, Ayling, and Beynon, J. Chem. Soc., 1936, 184.

<sup>&</sup>lt;sup>12</sup> Hinkel and Dunn, J. Chem. Soc., 1930, 1834.

<sup>&</sup>lt;sup>13</sup> Hinkel and Dunn, J. Chem. Soc., 1931, 3343.

<sup>&</sup>lt;sup>14</sup> Hinkel and Watkins, J. Chem. Soc., 1944, 647.

<sup>15</sup> Dains, Ber., 35, 2496 (1902).

<sup>&</sup>lt;sup>16</sup> Gattermann and Schnitzspahn, Ber., 31, 1770 (1898).

<sup>&</sup>lt;sup>17</sup> Neff, Ann., 287, 337 (1895).

reagent in these reactions, it must be able to utilize both its carbon atoms for the formation of aldehyde.

In any event the reaction apparently proceeds by the formation of the conjugate acid of hydrogen eyanide (V) or of one of a number of other possible ions, which, with the aid of aluminum ehloride, can serve as a

substituting agent in a reaction which is presumably analogous to Friedel-Crafts acylation. Certain reactions, however, proceed without the aid of aluminum chloride or other catalyst. Apparently the product from the Gattermann reaction is the conjugate acid VI or aluminum chloride complex VII of the aldimine or a more complex derivative of it. Generally the nitrogen-containing substance is not isolated but is hydrolyzed directly to the aldehyde.

A detailed discussion of the mechanisms must await a thorough study

of the kinetics of the reactions.

# SCOPE AND LIMITATIONS

# Ethers of Monohydric Phenols

A methylene formamidine adduct is formed by treating a mixture of a phenol ether, anhydrous aluminum chloride, and anhydrous hydrogen cyanide with anhydrous hydrogen chloride at approximately 40°.2 This adduct is readily hydrolyzed to the corresponding aldehyde. The following list illustrates those phenol ethers into which the aldehyde group has been introduced in yields of 80 to 100%:2,3,8 anisole, phenetole, o. and m-chloroanisole, m-chlorophenetole, the methyl and ethyl ethers of oand m-cresol, and the methyl ether of 1-naphthol. The aldehyde group enters the position para to the ether linkage unless the para position is occupied, when it enters the position ortho to the alkoxyl group. For example, p-cresyl methyl ether yields 2-methoxy-5-methylbenzaldehyde (80%).2,3 However, the preference of para substitution to ortho or occasional meta substitution is very strong both in the reactions with phenols and in the reactions with phenol ethers. The introduction of an aldehyde group into 2,4,6-trimethylanisole results in the formation of 3-hydroxy-2,4,6-trimethylbenzaldehyde (VIII) in only 5-10% yield along with small amounts of an unidentified hydroxydimethylbenzalde hyde. 18 Demethylation of the ether takes place concomitantly with the introduction of the aldehyde group. Other examples of demethylation of methyl ethers are given in the tables.

<sup>&</sup>lt;sup>18</sup> von Auwers and Mauss, Ber., 61, 1495 (1928).

With certain activated nuclei, hydrogen cyanide and hydrogen chloride may be used without a catalyst as in the preparation of the dialdehyde IX from the trimethylene ether of β-naphthol. Occasionally, zinc chloride

$$\begin{array}{c} \text{CHO} \\ \text{H}_3\text{C} \\ \text{CH}_3 \\ \text{VIII} \\ \\ \text{OR} \\ \text{VIII} \\ \\ \text{OR} \\ \text{CH}_3 \\ \text{CH}_3 \\ \\ \text{CH}_3 \\ \\ \text{CH}_3 \\ \\ \text{CH}_3 \\ \\ \text{OR} \\ \\ \text{CH}_3 \\ \\ \text{CH}_4 \\ \\ \text{CH}_5 \\ \\ \text{C$$

may be used to replace aluminum chloride advantageously, for example, with the methyl and ethyl ethers of 3,5-dimethylphenol (X).3 However, with few exceptions, aldehydes of monohydric phenol ethers can be prepared only with the use of aluminum chloride as a catalyst.

Attempts have been made to avoid the direct use of anhydrous hydrogen eyanide because of the hazard involved therein. Adams and his coworkers supplied a method whereby the phenol ether is treated in dry benzene with 2 equivalents of zinc eyanide. 5,6 After dry hydrogen chloride is passed through the solution to its saturation point,  $1\frac{1}{2}$  equivalents of anhydrous aluminum chloride are added and dry hydrogen chloride is again introduced at a temperature of approximately 40-45°. By the above procedure, excellent yields of anisaldehyde, 2-methoxy-5-methylbenzaldeliyde, and 2-methoxy-1-naphthaldeliyde have been reported; diphenyl ether gave p-phenoxybenzaldehyde in 50% yield.

Replacement of zinc cyanide by sodium or potassium cyanide or replacement of benzene by other solvents generally reduces the yields of Zirconium eyanide in the presence of zirconium ehloride aldehydes.6,9 in dry benzene gave only a poor yield of anisaldehyde from anisole under the conditions used.18a

# Monohydric Phenols

The procedure just described for introducing an aldehyde group into a phenol ether must usually be modified when introducing an aldehyde group into a monohydric phenol.<sup>3</sup> The phenol is treated with hydrogen eyanide in benzene, and the mixture is cooled with a salt-ice bath. Powdered aluminum chloride is slowly added, and the temperature is brought to 40° while anhydrous hydrogen chloride is introduced. phenol (30%), appear to vary with the structure of the phenol:3,19

<sup>&</sup>lt;sup>183</sup> Krishnamurti, J. Madras Univ., (1928) [C. A., 23, 2164 (1929)].

<sup>19</sup> Gattermann and Berchelmann, Ber., 31, 1765 (1898).

o-cresol (35-40%), m-cresol (45-50%), 2,3-dimethylphenol 2,5-dimethylphenol (80%), 3,5-dimethylphenol (quantitative), carvacrol (30%), m-chlorophenol (50%), m-bromophenol (10%), p-cresol (5%). Only one aldehyde group is introduced, and it always enters para to the hydroxyl group if that position is unoccupied. If the para position is blocked, the reaction may not proceed at all or it may lead in poor yield to a product in which the aldehyde group is ortho to the hydroxyl group. 2-Naphthol is an exception in that an excellent yield of 2-hydroxy-lnaphthaldehyde is obtained.3 2,3-Dimethylphenol yields 4-hydroxy. 2,3-dimethylbenzaldehyde (XI) in 60% yield with only a trace of the compound in which the aldehyde group has entered ortho to the hydroxyl 2,3,4-Trimethylphenol (XII), however, also yields 4-hydroxy group.3,18 2,3-dimethylbenzaldehyde (XI) as the chief product with only a trace of 2-hydroxy-3,4,5-trimethylbenzaldehyde (XIII), showing that the driving force towards para substitution is so strong that replacement of an alkyl group by an aldehyde group is preferred to ortho substitution. other examples of ring dealkylation are given in the tables.

Zinc chloride or the Adams modification may be substituted for aluminum chloride in the reactions with monohydric 2-naphthols that are unsubstituted in the 1-position and with 1-naphthols that are unsubstituted in the 4-position; the products containing the aldehyde group in the 1- and 4-position, respectively, are formed in almost quantitative yields.<sup>3,4</sup> In general, however, monohydric phenols fail to react unless aluminum chloride is added as a catalyst.<sup>6</sup> Using the Adams modification with aluminum chloride, the following phenolic aldehydes were prepared: 4-hydroxy-3-methylbenzaldehyde (38%), 4-hydroxy-5-isopropyl-2-methylbenzaldehyde (quantitative), 6,20,21 p-carvaerolaldehyde (good), 20,21 and 4-hydroxy-2-methylbenzaldehyde (30%).<sup>22</sup>

This explanation is supported by the fact that neither gallacetophenone (XIV) nor isopaeonol (XV) yields a  $\gamma$ -substitution product when treated with zine eyanide, hydrogen chloride, and aluminum chloride. When

γ substitution does occur yields are frequently excellent, e.g., 3-acetyl-2-hydroxy-4,6-dimethoxybenzaldehyde (84%),<sup>28</sup> 3,5-dicarbethoxy-2,4,6-tri-hydroxybenzaldehyde (85%),<sup>28</sup> 2,6-dihydroxy-3-propionylbenzaldehyde (64%),<sup>33</sup> 3-carbomethoxy-2,6-dihydroxybenzaldehyde (65%),<sup>29</sup> 3-carbalkoxy-2,6-dihydroxy-4-methylbenzaldehydes (quantitative).<sup>31</sup>

The Adams modification using zine cyanide and hydrogen chloride in the absence of aluminum chloride has also been successful in the preparation of aldehydes of polyhydric phenols having no nuclear deactivating substituents.  $^{5,36-40}$  Representative compounds prepared by this procedure follow:  $\beta$ -resorveylaldehyde (95%),  $^{5}$  2,4-dihydroxy-6-methylbenzaldehyde (85%),  $^{5}$  3-ethyl-2,4-dihydroxybenzaldehyde (74–80%), and 2,4-dihydroxy-3-methoxybenzaldehyde (93%). The formation of dialdehydes in low yields has been observed with phloroglucinol and its alkyl-substituted derivatives; phloroglucinol-3,5-dicarboxaldehyde is isolated from phloroglucinol in 1.5% yield. The yield of dialdehyde is increased to 6.6% with methylphloroglucinol and to 24% with ethylphloroglucinol.

Zinc chloride has been successfully substituted for aluminum chloride in a number of instances.<sup>3</sup>,<sup>23</sup>,<sup>41</sup>,<sup>42</sup> Its use with dihydric naphthols has been shown to result in the entrance of the aldehyde group into a free 1- or 4-position in the molecule in preference to a free 2-position.<sup>23</sup> Thus, 1,8-dihydroxynaphthalene when treated with hydrogen eyanide, hydrogen chloride, and zine chloride gives 4,5-dihydroxy-1-naphthaldehyde (24%) with only a very small amount of 1,8-dihydroxy-2-naphthaldehyde (0.8%). On the other hand, substitution in the 2-position is apparently favored

# Monoalkyl Ethers of Dihydric Phenols

In the monoalkyl ethers of resoreinol the aldehyde group usually enters para to the hydroxyl group rather than para to the alkoxyl group. For example, employment of Gattermann's procedure with aluminum chloride on the monomethyl ether of resoreinol results in a 75–80% yield of 4-hydroxy-2-methoxy-benzaldehyde.<sup>3,19</sup> In several instances, zinc chloride has been substituted for aluminum ehloride, as in the preparation of 6-hydroxy-3-methyl-2,3-dihydrobenzofuran-5-carboxaldehyde.<sup>51</sup> In this latter synthesis, the position para to the hydroxyl group is occupied and substitution occurs in the position para to the ether linkage.

# Polyalkoxy Derivatives of Benzene

The Gattermann procedure with aluminum chloride is effective for the introduction of the aldehyde group into polyalkoxybenzenes.<sup>2,3,52</sup> As with polyhydric phenols, the aldehyde group always enters para to an alkoxyl group if this position is available; resorcinol dimethyl ether is converted to 2,4-dimethoxybenzaldehyde in 80% yield by the Adams modification with added aluminum chloride.<sup>6</sup> Substitution may occur ortho to the alkoxyl group when the para position is blocked; e.g., the dimethyl and diethyl ethers of hydroquinone are reported to give 2,5-dialkoxybenzaldehydes in unspecified yields.<sup>3</sup>

When mixed ethers are subjected to the Gattermann reaction, a mixture of the possible isomeric aldehydes is formed.<sup>53,54</sup> Determination of the relative amounts of each has demonstrated the following order of influence by the alkoxyl group in directing the aldehyde group to the para position:<sup>53</sup>

# Molecules with Two Non-Fused Aromatic Nuclei

With molecules having two aromatic nuclei, each of which contains an ether linkage, it is possible to introduce an aldehyde group into each ring. The reaction has been applied to dimethylene and trimethylene ethers of phenol, o-cresol, m-cresol, 2,5-dimethylphenol, and 1- and 2-naphthol. The yields of dialdehydes vary from 30% to 75%.

Karrer, Glattfelder, and Widmer, Helv. Chim. Acta, 3, 548 (1920).

Gattermann and Eggers, Ber., 32, 289 (1899).
 Sonn and Patschke, Ber., 58, 1698 (1925).

<sup>14</sup> Unrasile and Orwall, J. Am. Chem. Soc., 65, 1736 (1943).

Similarly, 2,2'-dimethoxy- and 2,2'-diethoxy-biphenyl react to give the 5,5'-dialdehydes.<sup>3</sup> The corresponding 2,2'-dihydroxybiphenyl, however, is converted to dibenzofuran by the aluminum chloride, and only one aldehyde group is introduced.<sup>55</sup>

# Aromatic Hydrocarbons

Gattermann was unable to introduce the aldehyde group into aromatic hydrocarbons under the conditions he used. Tetralin was an exception, since it formed 3,4-tetramethylenebenzaldehyde in 33% yield. Gattermann often used benzene and other hydrocarbons as solvents in his reactions. It was later discovered, however, that an aldehyde group could be introduced into benzene provided that the conditions were modified so that free aluminum chloride was present.8 At 40°, in benzene, the complex of aluminum chloride with chloromethylene formamidine is not dissociated and reaction does not occur. If the temperature is raised to 80° or above, the complex appears to dissociate to some extent, yielding free aluminum chloride, and reaction does occur. If excess aluminum chloride is added, the yield of benzaldehyde is increased from 14% to 75%.8 It is advantageous to employ a mole-per-mole ratio of aluminum chloride to hydrogen eyanide when the aromatic compound is not very susceptible to polymerization; otherwise, the amount of aluminum chloride must be reduced and the time of reaction increased. The yields of aldehydes reported by Hinkel and his co-workers are based on the amount of hydrogen cyanide used instead of on the amount of aromatic compound as reported by Gattermann. On the assumption that 2 moles of hydrogen eyanide are required for every mole of aromatic compound converted to the aldehyde, the yields (which formerly were calculated to be only 50% based on the aromatic compound) actually correspond to yields of nearly 100% when a 1: I molar ratio of reactants was employed. It is certain, however, that 2 moles of hydrogen eyanide are not necessary for introduction of an aldehyde group into phenols and phenol ethers under all conditions.

<sup>&</sup>lt;sup>23</sup> Hinkel, Ayling, and Beynon, J. Chem. Soc., 1937, 778.

Just as the yield of benzaldehyde is markedly increased as the temperature is raised from that of the room to 100°,7 so the yield of aldehydes from other aromatic hydrocarbons is also increased. Unfortunately, the increase in temperature also increases the tendency for aluminum chloride to induce polymerization of the hydrocarbon. Hinkel and his co-workers recommend approximately 70° as the optimum temperature for most reactions.

Aldehydes can be prepared from liquid aromatic hydrocarbons by using excess hydrocarbon as the solvent; but, when the hydrocarbons are not liquid, are not easily procurable, or are unstable in the presence of aluminum chloride, the reaction must be modified by employment of inert solvents. Tetraehloroethane, o-dichlorobenzene, and chlorobenzene are suitable reaction media since they are good solvents for the hydrocarbons, hydrogen cyanide, and the final products, and since their high boiling points permit their use over a wide temperature range. Tetrachloroethane appears to promote the aldehyde synthesis, but it also increases the tendency of the aluminum ehloride to cause polymerization of the hydrocarbons. Indene is so readily polymerized that introduction of the aldehyde group has not been achieved.

Polymerization ean usually be reduced by employing a solvent with a lower chlorine content and by using but a slight excess of aluminum chloride, with a subsequent increase in the time of reaction. The effect of solvent is quite pronounced with biphenyl, which yields a monoaldehyde in chlorobenzene or o-dichlorobenzene, and a dialdehyde when the solvent medium is tetrachloroethane. Pertinent to the mechanism of the latter reaction is the fact that the monoaldehyde cannot be converted to the dialdehyde under the same conditions. A solvent effect has also been observed in the preparation of tolualdehydes from toluene; with excess toluene as solvent both m- and p-tolualdehyde are obtained, but with chlorobenzene as solvent only p-tolualdehyde is obtained. 56

A few of the aldehydes formed in good yields from the representative hydrocarbons as described by Hinkel and his co-workers are: benzaldehyde (75%), p-tolualdehyde (91%), 3,4-dimethylbenzaldehyde (85%), 2,4,6-trimethylbenzaldehyde (67-83%), 4-phenylbenzaldehyde (75%), fluorene-2-earboxaldehyde (76%), and acenaphthene-5-carboxaldehyde (70-90%),7,8,10,57

The Adams modification of the Gattermann reaction using zinc cyanide in the presence of aluminum ehloride was employed by Fuson and his co-workers for the preparation of some polyalkylated benzaldehydes.<sup>58,59</sup>

<sup>&</sup>lt;sup>24</sup> Niedzielski and Nord, J. Org. Chem., 8, 147 (1943).

Hinkel, Brit. pat. 397,124 (1933) [C. A., 28, 778 (1934)].
 Fuson, Horning, Rowland, and Ward, Org. Syntheses, Coll. Vol. III, 549 (1955).

Fuson, Horning, Ward, Rowland, and Marsh. J. Am. Chem. Soc., 64, 31 (1942).

Using tetrachloroethane as the solvent and a reaction temperature of 70°, 1,3,5-trialkylbenzenes are converted to 2,4,6-trialkylbenzaldehydes in 38-83% yield.

Complications that may be encountered with aromatic hydrocarbons are alkylation and alkyl migration; from ethylbenzene both mono- and di-ethylbenzaldehyde can be isolated.<sup>56</sup>

Sodium cyanide and hydrogen chloride with aluminum chloride have also been used. 9,56,60 This combination is generally applicable to aromatic hydrocarbons other than benzene. Aluminum chloride in excess of that required to form a 1:1 complex with chloromethylcne-formamidine is necessary. The yields of the corresponding aldehydes obtained from toluene and the isomeric xylenes appear to coincide with the polarity of the hydrocarbon reactants. Under these conditions, extensive migration and alkylation are observed so that some 2,4-dimethylbenzaldehyde is obtained from all three xylenes. The yields of this compound, however, vary with the xylene used: from o-xylene 75%, from m-xylene 26%, and from p-xylene 17%. In the reaction mixtures from m-xylene and p-xylene, 2,4,5-trimethylbenzaldehyde may be isolated in 13% and 21% yield, respectively; no trimethylbenzaldehyde is obtained from o-xylene. 56

### **Aromatic Amines**

The Gattermann reaction generally cannot be applied to aromatic amines. The preparation of *p*-aminobenzaldehyde by the reaction of hydrogen cyanide and hydrogen chloride on aniline in ether solution has been reported but not confirmed.<sup>61</sup> Hinkel and his eo-workers have obtained merely complex condensation products instead of aldehydes from aniline, dimethylaniline, and diphenylamine.<sup>55</sup>

# Pyrroles and Indoles

The aldehyde group is introduced with great case into certain pyrroles and indoles. This reaction proceeds so readily that frequently no catalyst is required. 62-65 Both diethyl ether and chloroform have been employed as solvents. The yields often vary with the solvent and have been considerably better in chloroform than in ether. 63 An outstanding example

<sup>66</sup> Mistritta and Nord, Nature, 145, 387 (1940).

<sup>&</sup>lt;sup>61</sup> Wu, J. Am. Chem. Soc., 66, 1421 (1944).

<sup>42</sup> Fischer and Ammann, Ber., 56, 2319 (1923).

<sup>42</sup> Fischer and Zerweck, Ber., 56, 519 (1923).

<sup>44</sup> Reichstein, Helv. Chim. Acta, 13, 349 (1930).

<sup>43</sup> Soka, Ber., 56, 2058 (1923).

is 2,3,5-trimethylpyrrole, which is converted in 67% yield to 2,4,5-trimethylpyrrole-3-carboxaldehyde in ehloroform solution but which apparently gives no product in diethyl ether.

Aldehyde groups have not been introduced into unsubstituted pyrrole or indole. 61,66 This failure has been explained as the result of the reaction of the intermediate aldimine hydrochloride with the pyrrole of indole to give complex, colored condensation products. 66 No difficulty is encountered in introducing the aldehyde group into 1-alkylpyrroles such as 1-methylpyrrole, 1-n-butylpyrrole, 1-i-amylpyrrole, and 1-furfurylpyrrole. 66 The aldehyde group enters the 2- or 5-position if one is free, but if both these positions are occupied, it may readily enter the 3- or 4-position. Another noteworthy fact is that the carbethoxy group and various acyl groups apparently do not prevent the reaction; many of the best yields of pyrrole aldehydes have been from pyrroles containing such substituents which are normally nuclear deactivating. In the absence of an open position, a carbethoxy group may be replaced by an aldehyde group. 67 The aldehydes from a selected list of pyrroles are given below with the yields obtained.

# Thiophenes and Thiazoles

Few applications of the Gattermann reaction in the thiophene series have been made. Thiophene is less reactive than furan and pyrrole, and the aldehyde group may be introduced (in poor yield) only in the presence of aluminum chloride. Undoubtedly, the tendency of thiophene to polymerize under acidic conditions is the chief obstacle to the application of the Gattermann reaction in this series.

2-Hydroxy-4-methylthiazole-5-carboxaldehyde (25%) is prepared by the use of hydrogen cyanide and hydrogen chloride in the absence of a catalyst, but 4-methylthiazole fails to react.<sup>76</sup>

### Enols

Ethyl acetoacetate dissolved in benzene is converted by hydrogen eyanide and hydrogen chloride in the presence of aluminum chloride into ethyl  $\alpha$ -formiminoacetoacetate hydrochloride.

$$\begin{array}{c} \mathrm{CH_{3}COCH_{2}CO_{2}C_{2}H_{5}} \xrightarrow{\mathrm{HCN,HCl,AlCl_{3},}} \mathrm{CH_{3}COCHCO_{2}C_{2}H_{5}} \\ \mathrm{CH} = \mathrm{NH\cdot HCl} \end{array}$$

Analogous results are obtained with acetylacetone, and, presumably, other active methylene compounds would act similarly. Simple olefins, however, do not yield the corresponding aldehydes under the conditions of the Gattermann reaction.<sup>78</sup>

# ALTERNATIVE METHODS FOR DIRECT INTRODUCTION OF AN ALDEHYDE GROUP

Several alternative methods for the direct introduction of aldehyde groups into aromatic compounds are available. The Gattermann-Koch reaction employing carbon monoxide, hydrogen chloride, and aluminum chloride, often with a cuprous chloride carrier, is used chiefly for the preparation of benzaldehyde and the mono- and poly-alkylbenzaldehydes. It is unsuccessful with phenols, phenol ethers, and heterocyclic compounds. 1,2

A second method employs N-methylformanilide and phosphorus oxychloride. It is limited to certain activated compounds such as ethers of the aromatic series, 79 secondary and tertiary aromatic amines, 80 and

<sup>76</sup> Ochiai and Nagasawa, Ber., 72, 1470 (1939).

<sup>77</sup> Wieland and Dorrer, Ber., 58, 818 (1925).
78 Wieland and D

Wieland and Dorrer, Ber., 63, 404 (1930).
 Kalischer, Scheyer, and Keller, German pats. 514,415 (1931), and 519,444 (1931).
 [Chem. Zentr., 102, II, 3394 (1931).]

<sup>80</sup> Vilsmeier and Haack, Ber., 60, 119 (1927).

chloride it reacts as desired.97 Zinc cyanide that has been washed thoroughly with water and dried does not react, but after addition of sodium chloride or potassium chloride it does react. The amount of catalyst usually used is slightly more than that needed for formation of the hydrogen cyanide adduct.

Solvents. Benzene is frequently used as a solvent particularly where aluminum chloride and a comparatively low reaction temperature are employed. With zinc chloride or in the absence of any catalyst, ether is a desirable solvent in view of its greater solvent action on polyhydric phenols. Furthermore, with ether as a solvent, the primary reaction product, the pure crystalline imine salt, may separate from solution and thus permit isolation before hydrolysis.11 Chloroform is preferable to ether for the reaction with certain substituted pyrroles. 63 The success of and the orientation obtained in the Gattermann reaction are frequently affected by the nature of the solvent.<sup>56</sup> Tetrachloroethane has been used frequently, as have o-dichlorobenzene and chlorobenzene since they dissolve hydrocarbons, hydrogen cyanide, and final products alike and have high boiling points.

Hydrogen Cyanide. Cylinders of anhydrous hydrogen cyanide can be purchased. The acid can also be prepared readily by treating sodium cyanide with sulfuric acid,98 or by treating potassium ferrocyanide with sulfuric acid followed by drying by passage over calcium chloride.99 Detailed directions for the preparation of hydrogen cyanide from sodium cyanide and sulfuric acid are given in Organic Syntheses. 100 Cyanogen bromide as a substitute for hydrogen cyanide appears to have little if any advantage.48

# EXPERIMENTAL PROCEDURES

Mesitaldehyde (hydrogen chloride, zinc cyanide, aluminum chloride, tetrachloroethane as solvent). Detailed directions for the preparation of mesitaldehyde in 75-81% yield from mesitylene are given in Organic Syntheses.58

4-Mcthoxy-3-methylbenzaldehyde (hydrogen cyanide, hydrogen chloride, aluminum chloride).2 Hydrogen cyanide is extremely poisonous and should be handled with great care. All connections should be thoroughly tested for leaks, and the entire apparatus should be placed in a hood which is in good working order. Rubber gloves should be worn. Adequate ventilation should be maintained at all times. Any vapors escaping from the system

<sup>97</sup> Arnold and Sprung, J. Am. Chem. Soc., 60, 1699 (1938).

<sup>33</sup> Ziegler, Ber., 54, 110 (1921).

<sup>33</sup> Houben, Ber., 59, 2878 (1926).

<sup>109</sup> Ziegler, Org. Syntheses, Coll. Vol. 1, 2nd ed., p. 314, John Wiley & Sons, 1941.

should not be allowed to escape freely, but should be destroyed by passage through solutions of potassium permanganate or hydrogen peroxide. Before handling hydrogen cyanide, one should consult textbooks on the handling of dangerous materials and the treatment and first aid of hydrogen cyanide poisoning.

Gaseous hydrogen chloride is passed for one-half hour through a mixture of 25 g. (0.93 mole) of anhydrous hydrogen cyanide and 30 g. (0.25 mole) of o-cresyl methyl ether cooled in an iee bath. Aluminum chloride, 30 g. (0.22 mole), is added gradually. While slowly adding more hydrogen chloride, the temperature is raised to 45° and kept there for four to five hours. The reaction mixture is poured over ice and hydrochloric acid. The resulting copious precipitate is heated under reflux with hydrochloric acid. The aldehyde is steam-distilled and then treated with sodium bisulfite solution. The bisulfite addition product is filtered and decomposed with aqueous sodium earbonate. The yield of colorless oil, b.p. 251°, is 30-37 g. (80-100%).

4-Hydroxy-2,6-dimethylbenzaldehyde (hydrogen chloride, hydrogen eyanide, aluminum chloride, benzene as solvent).<sup>3</sup> To an iee-cooled solution of 20 g. (0.16 mole) of 3,5-dimethylphenol in 80 ml. of benzene is added 13.8 g. (0.51 mole) of dry hydrogen eyanide. This is followed by 30 g. (0.22 mole) of aluminum chloride. After hydrogen ehloride has been passed through the mixture for four hours at a temperature of 35°, it is poured into a mixture of hydrochloric acid and ice. Benzene is removed by steam distillation, and the residue is extracted with ether. The resulting ethereal solution is extracted with sodium bisulfite solution. After the aqueous layer has been washed with ether, it is acidified with dilute sulfuric acid. The precipitated aldehyde is crystallized from ethanol in the form of long yellow needles, m.p. 189–190°, in an almost quantitative yield.

2-Hydroxy-1-naphthaldehyde (hydrogen chloride, hydrogen cyanide, zinc chloride, anhydrous ethyl ether as solvent). To a well-cooled mixture of 15 g. (0.10 mole) of 2-naphthol, 45 ml. of ether, and 6.9 g. (10 ml., 0.26 mole) of dry hydrogen cyanide is added 15 g. (0.11 mole) of anhydrous zinc chloride. Anhydrous hydrogen chloride is passed through this mixture at room temperature for two and one half hours. During this time a dark oil settles to the bottom and eventually solidifies. The solid is washed thoroughly with ether and then heated for a short time with water. The oily material, which crystallizes in almost quantitative yield on cooling, melts at 81° after crystallization from dilute ethanol.

2,4-Dihydroxybenzaldehyde (hydrogen chloride, hydrogen cyanide from potassium ferrocyanide and sulfuric acid, anhydrous ethyl ether as solvent). Potassium ferrocyanide (200 g.) is heated in a flask with a

mixture of 160 g. of concentrated sulfuric acid and 280 ml. of water. The evolved hydrogen cyanide is led from the flask by means of an air condenser and passed through a calcium ehloride drying train kept at 35–40° (hydrogen cyanide liquefies at 26°), and into a flask kept at —5° that contains 1 part of resorcinol dissolved in 3 parts of anhydrous ether. When the increase in weight indicates a 50% excess of hydrogen cyanide, hydrogen chloride is led slowly through the same drying train until it ceases to be absorbed by the ether solution. The semisolid reaction mixture is allowed to stand for several hours, after which it is decomposed with boiling water. The resulting mixture is filtered, and, on cooling, crystals of the aldchyde separate in good yield.

2,4-Dihydroxy-6-methylbenzaldehyde (hydrogen chloride, zinc cyanide, anhydrous ethyl ether as solvent).<sup>5</sup> A 500-ml. three-necked round-bottomed flask is fitted with a stirrer, a reflux condenser, and an inlet tube having a wide mouth to prevent clogging and extending nearly to the bottom of the flask. A safety bottle is placed in series with this tube and a dry hydrogen chloride generator. The top of the condenser connects to a tube leading into a wash bottle containing sulfuric acid, then to a safety bottle, and finally to the surface of aqueous sodium hydroxide. To the reaction flask, containing 20 g. (0.16 mole) of thoroughly dried orcinol (freed of water of crystallization) and 200 ml. of dry ether, is added 28.1 g. (0.24 mole) of dry zinc cyanide. The mechanical stirrer is started, and dry hydrogen chloride is passed in rapidly. A pink color develops, and the condensation product begins to separate as a thick oil. After about one and one half hours, the ether becomes saturated with hydrogen chloride; the hydrogen chloride is then passed in more slowly for an additional half hour. After the ether is decanted, the solid residue is boiled for two to three minutes with about 100 ml. of water. The hot solution is filtered and cooled to yield a crystalline product (85%) which, after crystallization from water, melts at 178–180°.

p-Anisaldehyde (hydrogen chloride, zinc cyanide, aluminum chloride, benzene as solvent).<sup>6</sup> The same type of apparatus may be employed for this preparation as was used above for the preparation of 2,4-dihydroxy-6-methylbenzaldehyde. To a mixture of 30 g. (30.1 ml., 0.28 mole) of anisole and 75 ml. of dry benzene is added 52 g. (0.44 mole) of dry zinc cyanide. Dry hydrogen chloride is added rapidly to the cooled and continuously stirred mixture for thirty to sixty minutes. Anhydrous aluminum chloride (49 g., 0.34 mole) is added slowly and with further cooling and stirring. This is followed by a slow stream of hydrogen chloride which is added while the mixture is heated at 40–45° for three to four hours. The contents of the flask are added to an excess of 10% hydrochloric acid, which generally causes a heavy precipitate to separate.

The resulting mixture is heated under reflux for one-half hour, and the aldehyde is steam-distilled. The steam distillate is extracted with benzene, and the benzene is subsequently removed by distillation. The residue is shaken with sodium bisulfite solution, and the anisole is extracted with ether. The aldehyde is released from the bisulfite addition product by warming with aqueous sodium earbonate. The yield of aldehyde, boiling at 246–248°, is 94%.

p-Tolualdehyde (hydrogen chloride, hydrogen cyanide, aluminum chloride, toluene as solvent).<sup>8</sup> To a mixture of 52 g. (0.39 mole) of aluminum chloride and 50 ml. of toluene cooled in ice is added with shaking 10.3 g. (15 ml., 0.38 mole) of dry hydrogen cyanide during a period of fifteen minutes. After being kept at room temperature for five minutes, the mixture is heated to about 60° and a slow current of hydrogen chloride is passed through. A vigorous reaction occurs, and the mixture is maintained at 100° for two hours while hydrogen chloride is introduced and an additional three hours at 100° after the flow of hydrogen chloride is stopped. The reaction mixture is kept at room temperature overnight. After the viseous mixture is poured over a mixture of ice and concentrated hydrochloric acid, the resulting organic layer is steam-distilled. From the dried ethereal extract of the distillate, the aldehyde is obtained in quantitative yield by fractional distillation; b.p. 200–204°.

3,5-Dimethylpyrrole-2-carboxaldehyde (hydrogen chloride, hydrogen cyanide, chloroform as solvent). To a solution of 4 g. (0.03 mole) of 2,4-dimethylpyrrole in 40 ml. of chloroform that has been previously dried with phosphorus pentoxide is added 5.5 g. (0.2 mole) of dry hydrogen cyanide. The mixture is cooled with an ice bath, and dry hydrogen chloride is introduced for one hour. Without attempting to filter the crystals, the solvent is removed under reduced pressure at room temperature, and the residue is dissolved in cold water. Sodium hydroxide is added, ammonia is evolved, and the aldehyde separates as dark yellow crystals of melting point 89°; yield, 92%.

# TABULAR SURVEY OF ALDEHYDES PREPARED BY THE GATTERMANN REACTION

In the following tables an attempt has been made to cover the syntheses of aromatic aldehydes by the Gattermann reaction reported in the literature to January 1, 1954. The first column in the tables lists the aldehydes formed, the second column the reagents and solvents, without parentheses. Also in the second column is listed in parentheses the starting material wherever it is not obvious.

Table I lists compounds obtained from aromatic hydrocarbons, chlorobenzene, and aniline. Usually the substituted benzaldehyde formed is

indicated merely by the substituent groups. Table II gives the aldehydes derived from phenols and phenol ethers; Table III lists the aldehydes obtained from naphthols, naphthol ethers, and phenanthrol. Heteroeyelie aldehydes are listed in Table IV; and compounds that did not yield aldehydes are shown in Table V.

The reagents are listed as A, B, C, D, E, and F as defined below:

A: HCl, HCN.

B: HCl, HCN, ZnCl2.

C: HCl, HCN, AlCl<sub>3</sub>.

D: HCl, NaCN, AlCl<sub>3</sub>.

E: HCl, Zn(CN)<sub>2</sub>, AlCl<sub>3</sub>.

F: HCl, Zn(CN)2.

Appreciation is expressed to Dr. O. L. Norman for his assistance in surveying the literature on which these tables are based.

TABLE I
ALDEHYDES PREFARED FROM AROMATIC HYDROCARBONS

Substituent(s) in Benzaldehyde or Complete Name of Aldehyde	Reagents	Yield, %	Reference
Benzaldeliyde	D	11	60
	C		57
		16-39	8
	C, CHCl <sub>2</sub> CHCl <sub>2</sub>	75	7
4-Amino-	A, ether (aniline)		61
4-Chloro-	C (manage)	8	7
4-Methyl-	D	39	9
1 2 20011 y 1 -	2	20	60
	C		57
	C	14-91	10
		14-quant.	8
4-Ethyl-	D	27	9
1-120113 1-	D	38	60
	C	30	56
	C, C <sub>6</sub> H <sub>5</sub> Cl	22	7
	C, CHCl <sub>2</sub> CHCl <sub>2</sub>	- <b>-</b> 5	7
4-Isopropyl-	D	24	60
4-s-Butyl	D	4	60
4-t-Amyl-	D	8	60
4-Phenyl-	C, CHCl <sub>2</sub> CHCl <sub>2</sub>	75	7
2,4-Dimethyl-	C		57
-,	C	97	8
	D	26	56
	D, (o-xylene)	75	56
	D, (p-xylene)	17	56
2,5-Dimethyl-	C	85	8
3,4-Dimethyl-	C	85	8
	D	42	9
Diethyl-	D, (ethylbenzene)	13	56
	C, (ethylbenzene)	25	56
2-Isopropyl-5-methyl-	D	25	56
Isopropyl-methyl-	D, (p-cymene)	5-17	56
Diisopropyl-	D, (isopropylbenzene)	12–18	9, 56
	D, $(m$ -diisopropylbenzene)	17–39	56
	D, (p-cymene)	13	56
3,4-Trimethylene-	C, CHCl <sub>2</sub> CHCl <sub>2</sub> (hydrindene)	45–60	7

TABLE I—Continued

ALDEHYDES PREPARED FROM AROMATIC HYDROCARBONS

Substituent(s) in Benzaldehyde or Cemplete Namo of Aldehydo	Reagents	Yield, %	Reference
3,4-Tetramethylene-	C, CHCLCHCl <sub>2</sub> (tetralin)	4	7
5,4.1 Colamony lene-	C, C <sub>6</sub> H <sub>6</sub> (tetralin)	33	3
2,3,5-Trimethyl-	D, (mesitylene)	13	56
2,4,5-Trimethyl-	D	7	56
2, 1,0-1111100-1,1	D, (m-xylene)	13	56
	D, (p-xylene)	21	56
2,4,6-Trimethyl-	C, CHCl <sub>2</sub> CHCl <sub>2</sub>	67-83	7
μ, 1, α-111110011 j 1·	E, CHCl <sub>2</sub> CHCl <sub>2</sub>	75-81	58, 59
	D, (1,2,4-trimethylbenzene)	7	56
2,4,6-Triethyl-	E, CHCl <sub>2</sub> CHCl <sub>2</sub>	69	58, 59
Triethyl-	D, (ethylbenzene)	5	56
Diisopropyl-methyl-	D, (p-eymene)	10-16	56
2,4,6-Triisopropyl-	E, CHCl <sub>2</sub> CHCl <sub>2</sub>	65	58, 59
Triisopropyl-	D, (m-diisopropylbenzene)	5-16	56
2-Fluoreneearbox-	D, (m-andopropyrodizone)	0 10	
aldehyde	C, CHCl <sub>2</sub> CHCl <sub>2</sub>	52-70	7
	C, C <sub>6</sub> H <sub>5</sub> Cl	76	7
	$C$ , $o$ - $C_6H_4Cl_2$	62	7
1-Naphthaldehyde	C, C <sub>6</sub> H <sub>5</sub> Cl	31-60	7
	C, CHCl <sub>2</sub> CHCl <sub>2</sub>	66	7
4-Methyl-1-naphth-	o, o <u>n</u> o <u>n</u>	00	
aldehyde	C, o-C <sub>6</sub> H <sub>4</sub> Cl <sub>2</sub>	51	7
2,3-Dimethyl-1-	-,,, -	0.	
naphthaldehyde	E, CHCl,CHCl,	38	59
2,6-Dimethyl-1-	2 2	00	
naphthaldehyde	C, C <sub>6</sub> H <sub>5</sub> Cl	60.	7
4,7-Dimethyl-I-	0 0	00	
naphthaldehyde	C, C <sub>6</sub> H <sub>5</sub> Cl	58	7
5-Acenaphthenecar	box-		
aldehyde	C, CHCl <sub>2</sub> CHCl <sub>2</sub>	70-90	7
9-Anthracenecarbo	x-		
aldehyde	C, CHCl <sub>2</sub> CHCl <sub>2</sub>	50	7
0.77	C, C <sub>6</sub> H <sub>5</sub> Cl	60	7
9-Phenanthrenecar	box-		
aldehyde	C, C <sub>6</sub> H <sub>5</sub> Cl	44	7

TABLE II

ALDEHYDES PREFARED FROM PHENOLS AND THEIR ETHERS

# A. Aldehydes Prepared from Monohydric Phenols or Their Ethers

Substituent(s) in Benzaldehyde or Complete Structural Formula	Rengents	Yield, %	Reference
4-Hydroxy-	C, C <sub>6</sub> H <sub>6</sub>	30	3, 19
4-Methoxy-	D	43	9
	C	45-89	2, 3, 8
	$Zr(CN)_2$ , $ZrCl_4$ , $C_6H_6$	Poor	18
	$E, C_6H_6$	94	6
4-Ethoxy-	C	80	2, 3
4-(β-Bromoethoxy)-	C, C <sub>6</sub> H <sub>6</sub>	50	3
4-Phenoxy-	C or E, C <sub>6</sub> H <sub>6</sub>	50-80	3, 6, 101
$(-CH_2OC_6H_4CHO-p)_2$	$C, C_6H_6$		3
$CH_2(-CH_2OC_6H_4CHO-p)_2$	$C, C_6H_6$	30	3
4-(4'-Methoxyphenoxy)-	$C, C_6H_6$	6	54
2-Bromo-4-hydroxy-	$C$ , $C_6H_6$	10	3
2-Bromo-4-ethoxy-	C, C <sub>6</sub> H <sub>6</sub>		3
2-Chloro-4-hydroxy-	$C, C_6H_6$	50	3
2-Chloro-4-methoxy-	$C, C_6H_6$		3
2-Chloro-4-ethoxy-	C, $C_6H_6$	80	3
3-Chloro-4-methoxy-	C	ca. 80	2
	$C, C_6H_6$		3
2-Hydroxy-4-methyl-	E, $C_6H_6$	Small	22
$2 ext{-Hydroxy-5-methyl-}$	$C_6H_6$	5	3
2-Methoxy-5-methyl-	$\mathbf{E}, \mathbf{C_6H_6}$	80	6
	C, with or without benzene	ca. 80	2, 3
2-Ethoxy-5-methyl-	$C_{i}$ $C_{6}H_{6}$	80	3
4-Hydroxy- $2$ -methyl-	$\mathbf{E}$ , $\mathbf{C_{6}H_{6}}$	30	22
	$C$ , $C_6H_6$	45-50	3, 19
	E, $C_6H_6$ (2-isopropyl-5-methylphenol)	Small	20
4-Methoxy-2-methyl-	C	ca. 80	2, 3
4-Ethoxy- $2$ -methyl-	C	90	2, 3 3
O-(CH <sub>2</sub> ) <sub>2</sub> -O	G G T	0-	ð
CH <sub>3</sub> CH <sub>3</sub>	C, C <sub>6</sub> H <sub>6</sub>	33	3

<sup>&</sup>lt;sup>101</sup> Slotta and Soremba, Ber., 68, 2059 (1935).

A. Aldehydes Prepared from Monohydric Phenols or Their Ethers-Gontinued

Substituent(s) in Benzaldehyde or Completo Struetural Formula	Reagents	Yield, %	Reference
4-Hydroxy-3-methyl-	C or E, C <sub>6</sub> H <sub>6</sub>	35–40	3, 6, 19
	E, C <sub>6</sub> H <sub>6</sub> (2-methyl-5-isopropylphenol)	Small	20
4-Hydroxy-3-ethyl-	C, C <sub>6</sub> H <sub>6</sub>	65	3
4-Methoxy-3-ethyl-	c	90	2, 3
4-Ethoxy-3-ethyl-	C	80	2, 3
4-( $\beta$ -Bromoethoxy)-3-ethyl-	C, C <sub>6</sub> H <sub>6</sub>	50	3
O-(CH <sub>2</sub> ) <sub>2</sub> -O CH <sub>3</sub>	C, C <sub>6</sub> H <sub>6</sub>	Almost quant.	3
сно сно о−(сн <sub>2</sub> ) <sub>3</sub> −о сн <sub>3</sub> сн <sub>3</sub>	C, C <sub>6</sub> H <sub>6</sub>	ca. 33	3
сно сно			
2-Hydroxy-3,4-dimethyl-	С	Small	18
2-Hydroxy-4,5-dimethyl-	$C$ , $C_6H_6$	_	3
2-Hydroxy-6-isopropyl-3-	-, -86		
methyl-	E, C <sub>6</sub> H <sub>6</sub>	Small	20
2-Hydroxy-3-isopropyl-	_, - <u>6—</u> 6	2111111	
6-methyl-	E, $C_6H_6$	Small	20
4-Hydroxy-2,3-dimethyl-	$C, C_6H_6$	60	3
•	C		18
	C, (2,3,4-trimethylphenol	) 52	18
4-Hydroxy-2,5-dimethyl-	C, C <sub>6</sub> H <sub>6</sub>	80	3
4·Hydroxy-5-isopropyl- 2-methyl-	C or E, C <sub>6</sub> H <sub>6</sub>	Almost	3, 6, 19,
4-Hydroxy-2-isopropyl-		quant	20, 21
5-methyl-	ССП		3
•	$C$ , $C_6H_6$ $E$ , $C_6H_6$	30	20, 21
$O - (CH_2)_2 - O$	11. O <sub>6</sub> 11 <sub>6</sub>	Good	20, 21
H <sup>2</sup> C CHO CHO CHO	C, C <sub>6</sub> H <sub>6</sub>	66	3
4-Hydroxy-2,6-dimethyl-	C, C <sub>6</sub> H <sub>6</sub>	Almost quan	3 t.

# A. Aldehydes Prepared from Monohydric Phenols or Their Ethers-Continued

Substituent(s) in Benzaldehyde or Complete Structural Formula	Reagents	Yield, %	Reference
4-Methoxy-2,6-dimethyl-	B. ether		3
4-Ethoxy-2,6-dimethyl-	B, ether	Almost quant.	3
4-Hydroxy-3,5-dimethyl-	$C_{\epsilon}C_{\epsilon}H_{\epsilon}$		3
• •	C, (2,6-dimethylanisole)	Main product	3
	C, C <sub>6</sub> H <sub>6</sub> (2,4,6-trimethylanisole)	~ <del>_</del>	18
4-Methoxy-3,5-dimethyl-	C	Poor*	3
4-Ethoxy-3,5-dimethyl-	C	Moderate*	3
2-Hydroxy-3,4,5-trimethyl-	С	Small	18
3-Hydroxy-2,4,6-trimethyl-	C, (mesityl methyl ether)	_	18

<sup>\*</sup> This reaction involved some cleavage of the ether group.

# B. Aldehydes Prepared from Dihydric Phenols or Their Ethers

Substituent(s) in Benzaldehyde or Complete Struetural Formula	Reagents	Yield, %	Reference
2,4-Dihydroxy-	A or F, ether	56–97	3, 5, 11, <sup>41</sup> , 43, 44
	HCONH <sub>2</sub> , POCl <sub>3</sub> , ether		50
	C	Almost	19
		quant.	
		69-82	8
	BrCN, HCl, ZnCl2, ether		48
4. Hydroxy-2-methoxy-	C, C <sub>6</sub> H <sub>6</sub>	75	3
	C	80	19
2,4-Dimethoxy-	C or E, C <sub>6</sub> H <sub>6</sub>	80-almost	3, 6
_, <u></u>	o or, ogg	quant.	
	C	ca. 80	2
2-Ethoxy-4-methoxy- and	B, ether	26 and	53
4-ethoxy-2-methoxy-	_,	32, resp	
2-Methoxy-4-n-propoxy-	B, ether	26 and	53
and 4-methoxy-2-n-propoxy	·	26, resp	١.
4-Allyloxy-2-methoxy- and	B, ether	32 and	53
2-allyloxy-4-methoxy-	·	16, resp	).
4-Benzyloxy-2-methoxy- and	B, ether	Total	53
2-benzyloxy-4-methoxy-	•	yield, 4	0
4-Methoxy-2-phenoxy- and	C, C <sub>6</sub> H <sub>6</sub>	Total	54
2-methoxy-4-phenoxy-		yield,	
		40-45	
2,5.Dimethoxy-	C, C <sub>6</sub> H <sub>6</sub>		3
2,5.Diethoxy-	C, C <sub>6</sub> H <sub>6</sub>		3
3,4-Dimethoxy-	C	ca. 80	2
B 4 751 13	С, С <sub>6</sub> Н <sub>6</sub>	60	3
3,4-Diethoxy-	$C_{\bullet}C_{6}H_{6}$	75	3
CH <sub>2</sub>			
ό CH₂	C, C <sub>6</sub> H <sub>6</sub>	_	3
CHO 4-Methoxy-3-phenoxy- and 4-(2'-methoxyphenoxy)-	C, C <sub>6</sub> H <sub>6</sub>	40-48	5 54

# B. Aldehydes Prepared from Dihydric Phenols or Their Ethers-Continued

Substituent(s) in Benzaldehyde or Complete Structural Formula	Reagents	Yield, %	Reference
2,4-Dihydroxy-3-ethyl-	F	_	37
	A, ether		46
2,4-Dihydroxy-3-formyl-	E, ether (2,4-dihydroxy- benzaldehyde)	10	28
2,4-Dihydroxy-3-nitro-	E, ether	_	26
3-Acetyl-2,4-dimethoxy-	C, ether	_	25
•	E, ether	80	32
2,4-Dihydroxy-5-methyl-	C, C <sub>6</sub> H <sub>6</sub>	90	3
2,4-Dihydroxy-5-ethyl-	C, C <sub>6</sub> H <sub>6</sub>	Almost quant.	3
5-Carbomethoxy-2,4-		_	
dihydroxy-	F, ether	53	102
H <sub>2</sub> C CHO	B, ether	_	51
2,4-Dimethoxy-5-methyl-	C, C <sub>6</sub> H <sub>6</sub>	Almost quant.	3
2,4-Dihydroxy-6-methyl-	A, ether	93	3, 41
	C	Quant.	2
	F, ether	85	5
4-Hydroxy-2-methoxy-6-			
methyl-	$C, C_6H_6$	_	3
2,4-Dimethoxy-6-methyl-	C, C <sub>6</sub> H <sub>6</sub>	63	3
3-Acetyl-2,6-dihydroxy-	C, ether	<del></del>	25
	E, ether	45	30
2,6-Dihydroxy-3-propionyl-	E, KCl, $CH_3CO_2C_2H_5$ , ether	64	33
3-n-Butyryl-2,6-dihydroxy-	E, KCl, $CH_3CO_2C_2H_5$ , ether	26	33
3-Benzoyl-2,6-dihydroxy-	E, KCl, $CH_3CO_2C_2H_5$ , ether	36	33
	C, ether		25
3-Carbomethoxy-2,6-dihydroxy-		ea. 30	24
	E, ether	65	29
2,6-Dihydroxy-3-nitro-	E, ether		26

# B. Aldehydes Prepared from Dihydric Phenols or Their Ethers-Continued

Substituent(s) in Benzaldehyde or Complete Structural Formula	Reagents	Yield, %	Reforence
4,5-Dimethoxy-2-methyl-	C, C <sub>6</sub> H <sub>6</sub>	Almost quant.	3
5-Ethoxy-4-methoxy-2-methyl-	C, C <sub>6</sub> H <sub>6</sub>	1-	3
Chloro-dihydroxy-	C, C <sub>6</sub> H <sub>6</sub>	Almost	3
2,6-Dihydroxy-3,5-dimethyl-	F, ether	quant.	39
Acetyl-2,6-dihydroxy-3- phenyl-	E, KCl, CH <sub>3</sub> CO <sub>2</sub> H <sub>5</sub> , ether	51	33
3-Acetyl-5-ethyl-2,6-dihydroxy-		38	32
3-Carbomethoxy-5-ethyl-			01
2,6-dihydroxy-	E, ether	57	31
3-Formyl-2,6-dihydroxy-4- methyl- or 3-formyl-2,4- dihydroxy-6-methyl-	E, ether (2,4-dihydroxy-6- methylbenzaldehyde)	<del></del>	27
difference of the state of the	E, KCl, ether (2,4-dihydroxy-6-methylbenzaldehyde)	11	28
3-Acetyl-2,6-dihydroxy-	onimiaen jac,	••	
4-methyl-	C, ether		25
3-Carbomethoxy-2,6-dihy-	E, ether	26	$\frac{32}{34}$
droxy-4-methyl- or carbethoxy- analog	E, other	Almost quant.	34
3-Ethyl-4,6-dihydroxy-			
2-methyl-	F, ether	51	39
2,5-Dihydroxy-3,4,6-			4
trimethyl-	E, C <sub>6</sub> H <sub>6</sub>	47	103
3,5-Diethyl-2,6-dihydroxy- 4-methyl-	F, ether	F0	39
5-Carbethoxy-2,4-dihydroxy-	r, coner	52	33
3,6-dimethyl-	E, ether	62	34
$OCH_3$ $OCH_3$		<b>-</b>	
	C, C <sub>6</sub> H <sub>6</sub>	_	3
$ m ^{CHO}$ $ m ^{CHO}$ $ m ^{CC_2H_5}$ $ m ^{OC_2H_5}$			
CHO CHO	C, C <sub>6</sub> H <sub>6</sub>	50	3
103 Smith and King, J. Am. Cher	m. Soc., 63, 1889 (1941).		

# C. Aldehydes Prepared from Trihydric and Tetrahydric Phenols or Their Ethers

Substituent(s) in Benzaldehyde	Reagents	Yield, %	Reference
2,3,4-Trihydroxy.	C, C <sub>6</sub> H <sub>6</sub>		
	B, ether		19
	F, ether	50	3, 41
2,4-Dihydroxy-3-methoxy-	F, ether	45	5
2,4,5-Trihydroxy-	B, ether	93	40
	D, ether	$\mathbf{Almost}$	
2,5-Dihydroxy-4-methoxy-	A 7 (m)	quant.	3, 41
2 Tryurux y-4,5-dimethowr	A, Zn(CN) <sub>2</sub> , ether	39	
4-Linoxy-2-hydroxy-5.	A, $Z_{n(CN)_2}$ , ether		35
methoxy-		85	35
5-Ethoxy-2-hydroxy-4-	A, Zn(CN) <sub>2</sub> , ether	0.0	
memoxy.		86	35
2,4,5-Trimethoxy-	A, Zn(CN) <sub>2</sub> , ether		
and the same of th	C, C <sub>6</sub> H <sub>6</sub>	71	35
2,4,6-Trihydroxy-		Very	52
Juloxy:	A, ether	good	
2,4-Dihydroxy-6-methoxy-	BrCN, HCl, ZnCl <sub>2</sub> , ether	$\mathbf{Good}$	3, 41
or 2,6-dihydroxy-4- methoxy-	, Mill <sub>2</sub> , ether	_	48
6-Ethoxy-2,4-dihydroxy-	$_{ m B,\ ether}$		
3-Ethyl-2,4,6-trihydroxy-	A, ether		
3-Formyl-2 4 C	A, ether	97	42
3-Formyl-2,4,6-trihydroxy-	F. ether (-1)		45
3-Aeetyl-2,4,6-trihydroxy-	F, ether (phloroglucinol) E, ether	78	47
•	-, coner	2	38
2,6-Dihydray	C, ether	32	28
2,6-Dihydroxy-4-methoxy- 3-methyl-	- y confer	51	32
4-Ethoxy-2,6-dihydroxy-3-methyl-	E, ether	_	25
3.Formyl-2.4-dib	A, ether	72	28
	E, ether (2,4-dihydroxy-6.	71	
6-Hydroxy-2,4-dimethoxy-	methoxybenzaldehyde)	13	45
3-methyl.			28
3-Formyl-2-hydroxy-4,6-	A		
dimethoxy.	E, ether (2-hydroxy-4,6.	56	
3-Acetyl-2-hydroxy-4,6-dimethoxy	dimethoxyhom	21 crude	45
dimethoxy.	J benzaldehvde)	- crude	28
	E, ether		-

# C. Aldehydes Prepared from Trihydric and Tetrahydric Phenols or Their Ethers—Continued

Substituent(s) in Benzaldehyde	Reagents	Yield, %	Reference
3-Formyl-2,4,6-trihydroxy-			
5-methyl-	A, ether (methylphloro- glucinol)	7	38
5-Ethyl-3-formyl-2,4,6- trihydroxy-	A, ether (ethylphloro- glucinol)	24	38
5-i-Amyl-3-formyl-2,4,6- trihydroxy- 3,5-Dicarbethoxy-2,4,6-	A, ether (i-amylphloro- glucinol)	15	38
trihydroxy-	E, KCl, ether	85 crude	28
2,4-Dihydroxy-3,6-	F, ether (1,4-dimethoxy-		36
dimethoxy-	2,6-dibenzoxybenzene)	79	36

TABLE IV

ALDEHYDES PREPARED FROM HETEROCYCLIC COMPOUNDS

Product	Reagents	Yield, %	Reference
	1 other	35	74
2-Furfural	A, ether	56	105
3-Methyl-2-furfural	A, ether	60	74
5-Methyl-2-furfural	A, ether	53	74
5-Ethyl-2-furfural	A, ether	12	105
3,5-Dimethyl-2-furfural	A, ether		74
-H <sub>2</sub> COCHO 2	A, ether	Poor	(#
6-Hydroxybenzofuran-5-			
carboxaldehyde	B, ether		51
6-Hydroxy-3-methylbenzo-			
furan-5-earboxaldehyde	B, ether		51
6-Hydroxy-3,4-dimethyl-	•		
benzofuran-5-earboxaldehyde	e B, ether		42
4,6-Dimethoxybenzofuran-	,		
7-earboxaldehyde	A, ether	9	75
2-Carbethoxy-4,6-dimethoxy-	11, 011101		
benzofuran-7-earboxaldehyd	le C, ether	90	75
bomonium 1-out bominating a	B, ether	72	75
Dibenzofuran-3-earboxaldehyo	·	81	55
Discussive of Boundary	(o,o'-dihydroxy- biphenyl)		
2-Thiopheneearboxaldehyde	C	8	64
1-Methylpyrrole-2-earbox-			
aldehyde	A, ether, $CHCl_3$	31	64
1-n-Butylpyrrole-2-earbox-			
aldehyde	A, ether	61	64
1-i-Amylpyrrole-2-carbox-			
aldehyde	A, ether	62	64
1-(2'-Furfuryl)-pyrrole-		-	
2-carboxaldehyde	A, ether	16	64
5-Phenylpyrrole-2-carbox-		20	
aldehyde	F, ether		. 72
5-Carbethoxypyrrole-2-	,		• •
carboxaldehyde	A, CHCl <sub>3</sub> , ether	28	64
3,4-Dimethylpyrrole-2-	3, 551142		
carboxaldehyde	A, ether		- 106
161 December 11 and 11	_		

Reichstein, Zschokke, and Goerg, Helv. Chim. Acta, 14, 1277 (1931).
 Fischer and Hofelmann, Ann., 533, 225 (1930).

TABLE IV
ALDEHYDES PREPARED FROM HITTEROCYCLIC COMPOUNDS

Produet	Reagents	Yield, %	Reference
2-Furfural	A, ether	35	74
3-Mothyl-2-furfurnl	A, ether	56	105
5-Methyl-2-furfural	A, ether	60	74
5-Ethyl-2-furfural	A, ether	53	74
3,5-Dimethyl-2-furfural	A, ether	12	105
$\left[-\mathrm{H_2C}\left[\mathrm{O}\right]_\mathrm{CHO}\right]_2$	A, ether	Poor	74
6-Hydroxybenzofuran-5-			
earboxaldehyde 6-Hydroxy-3-methylbenzo-	B, ether		51
furan-5-carboxaldehyde 6-Hydroxy-3,4-dimethyl-	B, ether		51
benzefuran-5-earboxaldehyde 4,6-Dimethoxybenzefuran-	B, ether	-	42
7-carboxaldehyde 2-Carbothoxy-4,6-dimethoxy-	A, ethor	9	75
benzofuran-7-earboxaldehydo		90	75
Dihangata	B, ether	72	75
Dibenzofuran-3-carboxaldehydo	(0,0'-dihydroxy.	81	55
2-Thiophenecarboxaldehydo 1-Methylpyrrole-2-earbox-	biphenyl) C	8	64
aldehyde 1-n-Butylpyrrole-2-earbox-	A, ether, $\mathrm{CHCl}_3$	31	64
aldehyde 1 <i>-i-</i> Amylpyrrole-2-earbox- aldehyde	A, ether	61	64
1-(2'-Furfuryl)-pyrrole- 2-earboxaldehyde	A, ether	62	64
5-Phenylpyrrole-2-carbox- aldehyde	A, ether	16	64
5-Carbethoxypyrrole-2- carboxaldehyde	F, ether		72
3,4-Dimethylpyrrole-2- carboxaldehyde	A, CHCl <sub>3</sub> , ethor	28	64
105 Point and T	A, ether		106

Reichstein, Zschokke, and Goerg, Helv. Chim. Acta, 14, 1277 (1931).
 Fischer and Höfelmann, Ann., 533, 225 (1930).

TABLE IV—Continued

ALDEHYDES PREPARED FROM HETEROCYCLIC COMPOUNDS

Product	Reagents	Yield, %	Reference
3,5-Dimethylpyrrole-2-			
carboxaldchyde	A, CHCl <sub>3</sub>	92	63
	A, ether	Moderate	63
	HCONH <sub>2</sub> , POCl <sub>3</sub>		50
4-Bromo-3,5-dimethylpyrrole-			
2-carboxaldeliyde	A, ether	22	67
4-Ethyl-3,5-dimethylpyrrole-			
2-carboxaldehyde	A, CHCl <sub>3</sub>	8	107
3-Carbethoxy-4,5-dimethyl-			
pyrrole-2-carboxaldehyde	A, ether	_	109
4-Carbethoxy-3,5-dimethyl-			
pyrrole-2-carboxaldehyde	A, ether	95	68
4-Acetyl-3,5-dimethylpyrrole-			
2-carboxaldeliyde	A, ether or CHCl <sub>3</sub>	65	62
5-Ethyl-3-methyl-4-propionyl-	_		
pyrrole-2-carboxaldeliyde	A, ether		109
$H_3C_{\parallel}$ $CH_3$	A, CHCl <sub>3</sub> , ether	35	106
OHC CH=C(CN)CO2CH3			
H			
2,4,5-Trimethylpyrrole-3-			
carboxaldehyde	A, CHCl <sub>2</sub>	67	63
5-Ethyl-2,4-dimethylpyrrole-			
3-carboxaldehyde	A, $H_2O$	77	108
5-Carbethoxy-2,4-dimethyl-	•		
pyrrole-3-carboxaldehyde	A, ether	85	69
-	HCONH <sub>2</sub> , POCl <sub>3</sub> ,		
	ether		50
4-Carbethoxy- $2,5$ -dimethyl-			
pyrrole-3-carboxaldehyde	A, ether	77	68
	HCONH <sub>2</sub> , POCl <sub>3</sub> ,		
	ether		50
4-Carbethoxy-1,2,5-trimethyl-	. \ _		
pyrrole-3-carboxaldehyde	A, ether	ca. 90	70
4-Carbethoxy-2,5-dimethyl-1-			
p-tolylpyrrole-3-carbox-	A (1	00.00	<b>5</b> 0
aldehyde	A, ether	80-90	70
<ul> <li>Fischer and Sehubert, Ber., 56,</li> <li>Fischer and Walach, Ann., 447,</li> </ul>			

109 Fischer and Klarer, Ann., 447, 48 (1926).

TABLE IV-Continued ALDERYDES PREPARED FROM HETEROCYCLIC COMPOUNDS

Product	Reagents	Yield, %	Referenc
1-Carbethoxy-1-phenyl-2,5-			
dimethylpyrrole-3-carbox- aldehydc	A, ether	80-90	70
2-Methylindole-3-carbox-		75	71
aldehyde	B, ether	•	73
	F, ether	10	• • •
	$A$ , $CHCl_3$	90	66
	A, other	87	65
2-Carbethoxyindole-3-			
carboxaldehyde	A, CHCl <sub>3</sub>	and.	66
•	F, other	83	73
2-Carbethoxy-7-methylindole-			_
3-carboxaldehyde	F, ether	Good	73
2-Hydroxy-4-methylthiazole-			
4-earboxaldchyde	A, ether, CHCl <sub>2</sub> CHCl <sub>2</sub>	25	76

TABLE V COMPOUNDS THAT DID NOT YIELD ALDEHYDES

Starting Material	Reference	Starting Material	Reference
Indene*	7	o-Methexybiphenyl†	55
Nitrobenzene†	55	Pyrrele*	64
2-Nitrophenol†	55	2-Carboxypyrrole*	64
Benzeie Acid†	55	2-Acetylpyrrole‡	64
Cinnamic Acid†	55	Indelo	66
Aniline†	55	Furfuryl methyl ether*	74
Diphenylamine†	55	Difurfuryl other*	74
N,N-Dimethylaniline†	55	2-Carbomethexy-4,7-di-	
Azebenzene†	55	methexy-6-hydrexy-	
Benzephenene†	55	benzefuran	36
Anthraquinene†	55	4-Methylthiazole‡	76
1,5-Dihydrexyanthra-		Benzefuran‡	74
quinene†	55	Ethyl 2-fureate;	74
o-Hydrexybiphenyl†	55	2-Acetylfuran‡	74

<sup>\*</sup> A polymeric solid was formed.
† The starting material was recovered or a polymeric solid was formed.
‡ The starting material was recovered.

## CHAPTER 3

## THE BAEYER-VILLIGER OXIDATION OF ALDEHYDES AND KETONES

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## University College of the West Indies, Jamaica

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## INTRODUCTION

In 1899, Baeyer and Villiger<sup>1</sup> showed that the oxidation of the alieyelie ketones menthone, tetrahydrocarvone (I), and eamphor with permonosulfuric acid led to the formation of laetones.

Further studies, using a variety of ketones or aldehydes and hydrogen peroxide or peracids in various media, have established that the oxidation represented by the following equation is of wide applicability.

$$\begin{array}{ccc}
R - C - R' & \xrightarrow{H_2O_2 \text{ or peracld}} & R - C - OR' \\
0 & & & & & & \\
\end{array}$$

This oxidation, the Baeyer-Villiger reaction, is the subject of this review. As the oxidation normally employs mild conditions, gives reasonable yields, and shows a high degree of selectivity, it has proved useful in a variety of both synthetic and degradative studies. Recent investigations have led to a better definition of favorable experimental conditions and have extended appreciably the scope of the reaction.

## MECHANISM OF THE REACTION

It is now generally agreed that the Baeyer-Villiger reaction is ionic in character. The favored reaction pattern was first outlined by Criegee in 1948.<sup>2</sup> It assumes that in the first instance addition of the peroxide to the carbonyl group yields a hydroxyperoxide (A). This dissociates to give an electron-deficient ion (B), which rearranges to C with cleavage of a carbon-carbon bond. The postulated carbonium ion C decomposes to the ester D in a normal way.

This mechanism has recently been the subject of detailed discussion by a number of authors.<sup>3-9</sup> The scheme accounts for the observation that in the oxidation of substituted acetophenones with perbenzoic acid the

<sup>&</sup>lt;sup>1</sup> Baeyer and Villiger, Ber., 32, 3625 (1899).

<sup>&</sup>lt;sup>2</sup> Criegee, Ann., 560, 127 (1948).

supported by the observation that fluorenone peroxide, formulated as IV, rearranged to the lactone V on heating.<sup>14</sup> There is now evidence that fluorenone peroxide is a molecular complex of fluorenone and fluorenone hydroperoxide.<sup>15</sup> There is no evidence for the existence of stable "oxoxides."

It has been postulated that hydroxyl radicals may participate in the oxidation by interacting with the enolic form of the ketone. It is unlikely that such a step is involved in the Baeyer-Villiger reaction, as many ketones that are not capable of enolization undergo the reaction. Also, in cases where it is established that attack on enols takes place, hydroxylation and not Baeyer-Villiger oxidation occurs. It has been shown that unsaturated ketones may undergo Baeyer-Villiger oxidation without the olefinic bonds being attacked. This would not be expected if free hydroxyl radicals were involved.

## SCOPE OF THE REACTION

Saturated Aliphatic Ketones. There is only one example of the Baeyer-Villiger oxidation of a simple ketone of the type RCH<sub>2</sub>COCH<sub>2</sub>R' to an ester. Methyl n-hexyl ketone gives n-hexyl acetate (VI) and its hydrolysis products on treatment with hydrogen peroxide in hydrofluoric acid.<sup>20</sup>

$$\text{CH}_3(\text{CH}_2)_5\text{COCH}_3 \xrightarrow{\text{H}_2\text{O}_2} \text{CH}_3(\text{CH}_2)_5\text{OCOCH}_3 + \text{CH}_3\text{CO}_2\text{H} + \text{CH}_3(\text{CH}_2)_5\text{OH}$$

It has been shown that hydrogen peroxide in the presence of sulfuric acid may oxidize such ketones to ketone peroxides and  $\alpha$ -ketols. Perbenzoic acid is said to have no significant action. However, as peracids have not yet been used under the most favorable conditions there is no decisive evidence that they will not react with these simple ketones.

- Wittig and Pieper, Ber., 73, 295 (1940).
- 15 Criegee, Schnorrenberg, and Becke, Ann., 565, 7 (1949).
- 18 Böeseken, Proc. Acad. Sci. Amsterdam, 33, 134 (1930) [C. A., 24, 3806 (1930)].
- 17 Kritchevsky and Gallagher, J. Biol. Chem., 179, 507 (1949).
- Karrer and Schneider, Helv. Chim. Acta, 30, 859 (1947).
- 19 Baxendale, Evans, and Park, Trans. Faraday Soc., 42, 155 (1946).
- Hudlecky, Chem. Listy, 45, 380 (1952) [C. A., 47, 8012 (1953)].
   Pastureau, Compt. rend., 140, 1592 (1905); Bull. soc. chim. France, [4] 5, 227 (1909).

22 Baeyer and Villiger, Ber., 33, 1569 (1900).

When ketones with the carbonyl group attached to at least one secondary carbon atom are treated with peracids, esters are formed. The secondary grouping rearranges in preference to a primary one. In the series of alicyclic methyl ketones from methyl cyclobutyl ketone to methyl cycloheptyl ketone, oxidation with perbenzoic acid gives yields of acetates ranging from 58 to 78%.<sup>23</sup>

Steroid alcohols with the hydroxyl group attached to C-17 may be prepared conveniently by the Baeyer-Villiger oxidation of 20-keto steroids, such as pregnan-3\alpha,12\alpha-diol-20-one diacetate (VII).

This method was first applied using persulfuric acid,<sup>24</sup> but low yields were sometimes obtained,<sup>25</sup> and alternative procedures for the preparation of C-17 alcohols appeared preferable.<sup>26</sup> However, it has been found that perbenzoic acid and monoperphthalic acid give higher yields, particularly when acid catalysts are present.<sup>27, 28</sup> Also, unlike the alternative procedures, which involve ozonization or nitrosation, the reaction may be applied to unsaturated ketones such as pregnenolone.

The oxidation has been used as the key step in a degradation of sar-sapogenin (VIII) to pregnan-3,16,20-triol (IX).<sup>29</sup>

<sup>&</sup>lt;sup>23</sup> Friess and Pinson, J. Am. Chem. Soc., 74, 1302 (1952).

<sup>&</sup>lt;sup>24</sup> Marker and eo-workers, J. Am. Chem. Soc., 62, 650, 2543, 2621, 3003 (1940).

<sup>25</sup> Koeehlin and Reichstein, Helv. Chim. Acta, 27, 549 (1944).

<sup>&</sup>lt;sup>26</sup> Fieser and Fieser, Natural Products Related to Phenanthrene, 3rd ed., p. 400, Reinhold Publishing Corp., 1949.

<sup>&</sup>lt;sup>27</sup> Sarett, J. Am. Chem. Soc., 69, 2899 (1947).

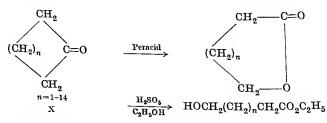
<sup>&</sup>lt;sup>28</sup> Wieland and Mieseher, Helv. Chim. Acta, 32, 1768 (1949).

<sup>&</sup>lt;sup>29</sup> Marker, Rohrmann, Crooks, Whittle, Jones, and Turner, J. Am. Chem. Soc., 62, 525 (1940).

$$\begin{array}{c} \text{CH}_3\\ \text{CHC}(\text{CH}_2)_2\text{CH}(\text{CH}_3)\text{CH}_2\text{OH} \\ \text{OH} \\ \text{OH} \\ \text{CHOCO}(\text{CH}_2)_2\text{CH}(\text{CH}_3)\text{CH}_2\text{OH} \\ \text{CHOCO}(\text{CH}_2)_2\text{CH}(\text{CH}_3)\text{CH}_2\text{OH} \\ \text{OCOCH}_3 \\$$

The value of the Baeyer-Villiger reaction in this series is enhanced by decisive evidence that rearrangement occurs with retention of configuration.<sup>7, 30, 31</sup> This fact has been utilized in the preparation of 2-decalols and C-17 hydroxy steroids of definite configuration.<sup>32</sup>

Alicyclic Ketones. Alicyclic ketones ranging from cyclobutanone to cycloheptadecanone  $(X, n = 14)^5$ , 33, 34 have been oxidized under Baeyer-Villiger conditions. The reaction provides a convenient method for determining structure and for preparing relatively inaccessible lactones and hydroxy acids. When persulfuric acid or hydrogen peroxide-hydrofluoric acid<sup>20</sup> is used for the oxidation, polyesters of the hydroxy acids are obtained. The ethyl esters of the simple hydroxy acids are formed when ethanol is present.<sup>35</sup> Organic peracids give excellent yields of lactones.



<sup>&</sup>lt;sup>30</sup> Mislow and Brenner, J. Am. Chem. Soc., 75, 2319 (1953).

<sup>31</sup> Gallagher and Kritschevsky, J. Am. Chem. Soc., 72, 882 (1950).

<sup>32</sup> Dauben and Hoerger, J. Am. Chem. Soc., 73, 1505 (1951).

Friess and Frankenburg, J. Am. Chem. Soc., 74, 2679 (1952).
 Ruzicka and Stoll, Helv. Chim. Acta, 11, 1159 (1928).

<sup>35</sup> Robinson and Smith, J. Chem. Soc., 1937, 371.

The oxidation has also been carried out under alkalinc conditions but the yields recorded are low.36-38

In the steroid series the procedure has been applied to compounds having earbonyl groups at C-3,28,39-43 C-7,44 and C-17.45,46 It has been demonstrated that conditions suitable for the oxidation of such compounds do not lead to any action on C-1127 or C-1240 carbonyl groups, although oxidation at C-12 does occur when a large excess of peracid is used. There is evidence that oxidation of the C-3 carbonyl group of cholestan-3-one and coprostan-3-one with persulfuric acid is inhibited by the presence of bromine in the 2- or 4-positions, 47 but that is not the case when excess perbenzoic acid is employed.28 The oxidation of androstan-3-one (XI) gives the lactone XII.43 7-Ketocholestan-3β-ol (XIII) is oxidized to the lactone XIV.44

In the oxidation of 17-keto steroids there is some doubt as to which bond adjacent to the carbonyl group is broken, but the evidence available favors the formulation XV for the lactone. 46

- <sup>36</sup> Westerfield, J. Biol. Chem., 143, 177 (1942).
- 37 Fling, Minard, and Fox, J. Am. Chem. Soc., 69, 2467 (1947).
- 38 Heine and Jones, J. Am. Chem. Soc., 73, 1361 (1951).
- 39 Gardner and Godden, Biochem. J., 7, 588 (1913).
- 40 Burckhardt and Reichstein, Helv. Chim. Acta, 25, 1434 (1942).
- 41 Ruzicka, Prelog, and Meister, Helv. Chim. Acta, 28, 1651 (1945).
- 42 Salamon, Z. physiol. Chem., 272, 61 (1941).
- Salamon, Z. physiol. Unem., 224, 92 (1945).
   Prelog, Ruzicka, Meister, and Wieland, Helv. Chim. Acta, 28, 618, 1651 (1945).
- 44 Heusser, Segre, and Plattner, Helv. Chim. Acta, 31, 1183 (1948).
- 45 Jacobsen, J. Biol. Chem., 171, 61 (1947).
- 46 Picha, J. Am. Chem. Soc., 74, 703 (1952).
- <sup>47</sup> Marker, J. Am. Chem. Soc., 62, 2543 (1940).

Aromatic Ketones. The oxidation of diaryl ketones with peracids regularly leads to the formation of esters or their hydrolysis products. Although this reaction is of little value as a preparative procedure, it does provide a convenient means of establishing the structures of polysubstituted benzophenones and alkyl aryl ketones.<sup>48</sup> The method is less drastic and more specific than the degradation procedures involving alkali fusion<sup>49</sup> or acid hydrolysis<sup>50</sup> that have been applied to natural products.

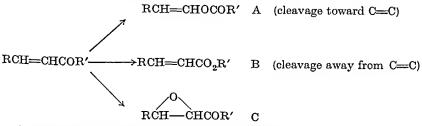
In the cleavage of unsymmetrical ketones the migrating group is normally the more electron-releasing one. Substituents in the aromatic nuclei influence the course of reaction in a manner similar to that observed in normal nucleophilic aromatic substitution. Thus treatment of p-incthoxybenzophenone with peracetic acid gives benzoic acid and hydroquinone monomethyl ether, while cleavage of p-nitrobenzophenone gives p-nitrobenzoic acid and phenol exclusively.<sup>4</sup>

Insufficient information is available to make it possible to predict the course of reaction of alkyl aryl ketones with certainty. Treatment with peracids and hydrogen peroxide in acid or neutral solution may lead to the migration of either the aromatic or the aliphatic group. Thus, with peracetic acid, acetophenone gives a mixture of esters, and eyelohexyl phenyl ketone gives esters XVI and XVII in the approximate proportion of  $5:1.^{21}$ 

However, in one study of the oxidation of meta- and para-substituted acetophenones with perbenzoic acid, acetates alone were obtained in good yields.<sup>10</sup>

Alkyl aryl ketones containing hydroxyl groups in the *ortho* or *para* position are converted to polyhydric phenols by hydrogen peroxide in alkaline solution. The yields are poor.<sup>52</sup>

 $\alpha,\beta$ -Unsaturated Ketones. The application of the Baeyer-Villiger reaction to this group of compounds should lead to reaction according to either A or B. Another possibility is preferential attack at the olefinic linkage leading to an  $\alpha,\beta$ -epoxyketone (C).



Although only a limited number of cases have been studied, examples of the formation of all three types of compound are available. The oxidation of benzalacetone (XVIII) with peracetic acid leads exclusively to the ester XIX.53

An  $\alpha$ -phenyl- $\alpha,\beta$ -unsaturated ketone (XX) gives a mixture of epoxyketone and the ester XXI.<sup>54</sup>

$$\begin{array}{c} \text{RCH} = \text{C}(\text{C}_6\text{H}_5)\text{COCH}_3 \rightarrow \text{RCH} = \text{C}(\text{C}_6\text{H}_5)\text{CO}_2\text{CH}_3 + \text{RCH} - \text{C}(\text{C}_6\text{H}_5)\text{COCH}_3 \\ \text{XXI} \\ \end{array}$$

Oxidation of  $\Delta^{16}$ -20-ketosteroids with perbenzoic acid leads to preferential attack at the olefinic linkage. Pregna-5,6-dien-3 $\beta$ -ol-20-one acetate has been converted in this way to 16,17-epoxypregna-5-en-3 $\beta$ -ol-20-one acetate, a useful intermediate in the preparation of 17 $\alpha$ -hydroxyprogesterone.

When  $\alpha,\beta$ -unsaturated ketones are treated with hydrogen peroxide in alkaline solution, epoxyketones are formed. There is no evidence of the Baeyer-Villiger reaction occurring under these conditions.

<sup>52</sup> Dakin, Am. Chem. J., 42, 474 (1909).

<sup>53</sup> Böeseken and Soesman, Rec. trav. chim., 52, 874 (1933).

<sup>&</sup>lt;sup>54</sup> Wenkert and Rubin, Nature, 170, 708 (1952).

<sup>55</sup> Julian, Meyer, and Ryden, J. Am. Chem. Soc., 72, 367 (1950).

Kohler, Richtmeyer, and Hester, J. Am. Chem. Soc., 53, 213 (1931).
 Fieser and co-workers, J. Am. Chem. Soc., 61, 3216 (1939); 62, 2866 (1940).

<sup>58</sup> Barkley, Farrar, Knowles, and Raffelson, J. Am. Chem. Soc., 75, 4110 (1953).

Polycarbonyl Compounds. α-Diketones and α-keto acids react readily with Baeyer-Villiger reagents. 59-64 In inert solvents anhydrides are formed,65-67 while in alkaline or acidic media simple carboxylic acids are generally produced in good yields. It would appear from some comparisons of conditions that higher yields are obtained when the oxidations are conducted in alkaline solution.68

The oxidation has been used in establishing structure and in the preparation of relatively inaccessible carboxylic acids. As typical examples, 9,10-diketostearic acid is converted quantitatively to azelaic and pelargonie acid,61

$$\begin{array}{c} {\rm CH_3(CH_2)_7COCO(CH_2)_7CO_2H} \ + \ {\rm CH_3CO_3H} \ \to \\ {\rm CH_3(CH_2)_7CO_2H} \ + \ {\rm HO_2C(CH_2)_7CO_2H} \end{array}$$

and phenanthraquinone forms diphenic acid. 69, 70

Unsaturated a-dikctones react in a similar manner. Treatment of 4-methyl-o-benzoquinone (XXII) with monoperphthalic acid gives β-methylmuconic anhydride XXIII.65

Dicinnamylidenebiacetyl (XXIV) is oxidized to the anhydride XXV,65

$${\rm C_6H_5(CH=\!CH)_2COCO(CH=\!CH)_2C_6H_5}$$
  $\rightarrow$  XXIV

$$C_6H_5(CH=CH)_2CO_2CO(CH=CH)_2C_6H_5$$

- 29 French and Sears, J. Am. Chem. Soc., 70, 1279 (1948).
- 40 Holleman, Rec. trav. chim., 23, 170 (1904).
- 41 Boeseken and Sloof, Rec. trav. chim., 49, 91 (1930).
- 42 Reistort, Ber., 30, 1041 (1897).
- 42 Weitz and Scheffer, Ber., 54, 2327 (1921).
- 44 Bjorklund and Hatcher, Trans. Roy. Soc. Can., (111), 44, 25 (1950) [C. A., 45, 7951 (1951)].
  - 41 Karrer, Schwyzer, and Neuwirth, Helv. Chim. Acta, 31, 1210 (1948).
  - 66 Karrer, Cochand, and Neuss, Helv. Chim. Acta, 29, 1836 (1946).
  - 67 Karrer and Hohl, Helv. Chim. Acta, 32, 1932 (1949). 41 Meyer, Hele, Chim. Acta, 30, 1976 (1947).
  - 19 Linstead and Walpole, J. Chem. Soc., 1939, 855.
  - 10 Perkin, Proc. Chem. Soc., 23, 165 (1907).

and puberulic acid (XXVI), presumably reacting through the keto form, is oxidized to aconitic acid (XXVII),71

The oxidation of  $\alpha$ -diketones normally involves cleavage between the carbonyl groups. However, it has been shown that the reaction of 2,2',4,4'-tetranitrobenzil with alkaline hydrogen peroxide gives 2,4-dinitrophenol and not 2,4-dinitrobenzoic acid which is formed in an acidic medium.<sup>72</sup>

The oxidation of 1,3-diketones and  $\beta$ -keto acids with peracids does not follow the normal pattern of the Bacyer-Villiger reaction. Treatment of dibenzoylmethane derivatives with perbenzoic acid leads to the formation of the corresponding dibenzoylcarbinols.<sup>73-76</sup>

$$\mathrm{C_6H_5COCH_2COC_6H_5} \ \rightarrow \ \mathrm{C_6H_5COCH(OH)COC_6H_5}$$

In an earlier study<sup>77</sup> it was found that an equimolecular amount of peracetic acid oxidized 1,3-diketones or  $\beta$ -keto acids to an acid and an alcohol. With excess peracetic acid a mixture of acids is formed. The first reaction was interpreted as involving migration of the group R' lying between the carbonyl groups.

$$\begin{split} & \text{RCOCH}(\text{R}')\text{COR}'' + \text{CH}_3\text{CO}_3\text{H} \rightarrow \text{RR}'\text{CHOH} + \text{R}''\text{COCO}_2\text{H} \\ & \text{R=\!CH}_3, \text{ C}_2\text{H}_5, \text{ C}_5\text{H}_{11}; \text{ R}'=\!\!\text{H, CH}_3, \text{ C}_6\text{H}_5\text{CH}_2; \text{ R}''=\!\!\text{CH}_3, \text{ OC}_2\text{H}_5 \end{split}$$

When  $\beta$ -triketones such as 2-acetylindan-1,3-dione (XXVIII) are treated with hydrogen peroxide in diethyl ether there is preferential oxidation of the acyl side chain leading to the formation of an ester (XXIX). In acidic or alkaline media, hydrogen peroxide oxidizes 2-acetylindan-1,3-dione to a mixture of acetic and phthalic acids.

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<sup>&</sup>lt;sup>71</sup> Corbett, Hassall, Johnson, and Todd, Chemistry & Industry, 1949, 626.

<sup>&</sup>lt;sup>72</sup> Blatt and Rytina, J. Am. Chem. Soc., 72, 403 (1950).

Blatt and Hawkins, J. Am. Chem. Soc., 58, 81 (1936).
 Karrer, Albers-Schonberg, and Kebrle, Helv. Chim. Acta, 35, 1498 (1952).

<sup>75</sup> Karrer, Kebrle, and Thakkar, Helv. Chim. Acta, 33, 1711 (1950).

<sup>76</sup> Karrer, Kebrle, and Albers-Schonberg, Helv. Chim. Acta, 34, 1014 (1951).

<sup>77</sup> Böeseken and Jacobs, Rec. trav. chim., 55, 804 (1936).

<sup>78</sup> Hassall, J. Chem. Soc., 1948, 50.

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$$\begin{array}{c} & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

The Bacyer-Villiger reaction has been used in the elucidation of the structure of the natural product leptospermone (XXX).<sup>79</sup>

Aldehydes. Peracids generally convert both aliphatic and aromatic aldehydes to earboxylic acids. 80-83 Hydrogen peroxide reacts with aliphatic aldehydes in neutral media to give hydroxyhydroperoxides. 84, 11 It is significant, however, that such peroxides rearrange readily on heating to give a mixture of the corresponding earboxylic acid and the formate of the next lower alcohol. This behavior suggests that the oxidation of aldehydes with peroxides normally follows the Baeyer-Villiger pattern.

The oxidation of citral (XXXI) to the lower aldehyde XXXII is an example of a similar course of reaction.<sup>85</sup>

11 Prilejneff, Bull. soc. chim. France, [4] 42, 687 (1927).

<sup>19</sup> Briggs, Hassall, and Short. J. Chem. Soc., 1945, 706.

<sup>&</sup>lt;sup>63</sup> D'Ans and Kneip, Ber., 48, 1136 (1915).

<sup>41</sup> Wieland and Richter, Ann. 495, 284 (1932).

Lyubarskii and Kagan, J. Phys. Chem., 39, 847 (1935).
 Ross, Gebbars, and Constant.

Ross, Gebhart, and Gerecht, J. Am. Chem. Soc., 67, 1275 (1945).
 Rusche, Alkylperaryde und Ozonide, p. 36, Steinkopf, Leipzig, 1931.

$$(\mathrm{CH_3})_2\mathrm{C} = \mathrm{CH}(\mathrm{CH_2})_2\mathrm{C}(\mathrm{CH_3}) = \mathrm{CH}\mathrm{CHO} \qquad \xrightarrow{\mathrm{C_6H_5CO_3H}}$$

$$\times \times \times \times \times \times$$

$$(\mathrm{CH_3})_2\mathrm{C} = \mathrm{CH}(\mathrm{CH_2})_2\mathrm{C}(\mathrm{CH_3}) = \mathrm{CH}\mathrm{OCHO} \rightarrow$$

$$(\mathrm{CH_3})_2\mathrm{C} = \mathrm{CH}(\mathrm{CH_2})_2\mathrm{CH}(\mathrm{CH_3})\mathrm{CHO} + \mathrm{HCO_2H}$$

$$\times \times \times \times \times \times \times$$

The oxidation of aliphatic aldehydes with hydrogen peroxide in acid and alkaline solution occasionally leads to the formation of hydrogen and hydrocarbons in addition to carboxylic acids.<sup>86–89</sup> Such reactions appear to involve a radical mechanism in addition to the normal ionic process.

Aromatic aldehydes have been oxidized with peroxides in a variety of media. In neutral or acid solution the action of peracids and hydrogen peroxide resembles that with alkyl aryl ketones under similar conditions. 90, 91 Benzaldehyde reacts with hydrogen peroxide in ether to give benzoic acid and only traces of phenol. 92 In aldehydes with electron-releasing substituents such as alkoxyl, hydroxyl, and amino 93 in the ortho or para positions, the formyl group tends to migrate, producing formates or phenols according to the conditions employed.

The oxidation of aromatic aldehydes in alkaline solution was first studied by Dakin, 52 who indicated that the reaction occurred only when hydroxyl groups were present in the *ortho* or *para* positions. In such cases good yields of polyhydric phenols are obtained through the replacement of formyl by hydroxyl groupings. As Table VI indicates, the Dakin procedure has been applied successfully to a variety of substituted phenolic aldehydes. It has been used for the synthesis of phenols such as morphol<sup>94</sup> (XXIII) which are not readily accessible by other means.

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<sup>&</sup>lt;sup>86</sup> Payne and Lemon, J. Am. Chem. Soc., 63, 226 (1941).

<sup>87</sup> Fry and Payne, J. Am. Chem. Soc., 53, 1973 (1931).

<sup>88</sup> Bezzi, Gazz. chim. ital., 63, 345 (1933).

<sup>89</sup> Bach and Generosov, Ber., 55, 3560 (1922).

<sup>90</sup> Böeseken and Greup, Rec. trav. chim., 58, 528 (1939).

<sup>91</sup> Waeek and Bezard, Ber., 74, 845 (1941).

<sup>92</sup> Spath, Pailer, and Gergeley, Ber., 73, 935 (1940).

<sup>&</sup>lt;sup>\$3</sup> Bamberger, Ber., 38, 2042 (1903).

<sup>34</sup> Barger, J. Chem. Soc., 113, 218 (1918).

It is of interest that the aldehydes XXXIV and XXXV, in which there is a nitro group ortho to the hydroxyl, are not attacked, while the aldehydes XXXVI and XXXVII react in the normal way. 52 The inhibiting effect

is probably due to intramolecular hydrogen bonding. It has been suggested that the Dakin oxidation follows a different course from the Baeyer-Villiger reaction, 95 but this has not been substantiated. 91

Side Reactions. Structural elements other than carbonyl groups may be attacked under the conditions used for the Baeyer-Villiger reaction. The susceptibility of olefinic linkages to oxidation by peracids is well known.96 Aromatic hydrocarbons, such as mesitylene, 97 methylcholanthrene, and benzpyrene,98 which are particularly sensitive to attack by electrophilic reagents, may be oxidized preferentially. The reactivity of other groupings was reviewed in 1949.99

There are some isolated examples of oxidation of the normal products of reaction by Baeyer-Villiger reagents. For example, phenols may react with peracids, 100-102 and demethylation of aromatic ethers may occur. 102 Catechols and hydroquinones may be oxidized through quinones to carboxylic acids. 103, 104 However, if a large excess of reagent is avoided it is generally possible to obtain substantial yields of phenols from Baeyer-Villiger reactions. 48 In one example of the Dakin reaction, the oxidation of 2-hydroxy-5-methoxybenzaldehyde, the formation of an unidentified, abnormal product has been reported.105

There is evidence, in two cases, of oxidation of secondary alcohols by the action of excess peracetic acid. When 1,3-diketones react with excess of this peracid, a ketone is obtained in the place of the secondary alcohol produced with an equimolar amount.77 The steroid hydroxy ketone

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<sup>95</sup> Wacek and Eppinger, Ber., 73, 644 (1940).
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<sup>56</sup> Swern, Org. Reactions, 7, 378 (1953).

<sup>97</sup> Friess and Miller, J. Am. Chem. Soc., 72, 2611 (1950).

<sup>14</sup> Eckhardt, Ber., 73, 13 (1940).

<sup>50</sup> Swern, Chem. Revs., 45, 1 (1949).

<sup>182</sup> Bosseken and Engelberts, Proc. Acad. Sci. Amsterdam, 34, 1202 (1931) [C. A., 26, 2070

<sup>101</sup> Fernholz, Chem. Ber., 84, 110 (1951).

<sup>1</sup>et Friest, Soloway, Morse, and Ingersoll, J. Am. Chem. Soc., 74, 1305 (1952).

<sup>141</sup> Wacek and Fiedler, Monaish., 80, 170 (1949). <sup>101</sup> Weitz, Schobbert, and Scibert, Ber., 68, 1163 (1935).

<sup>191</sup> Resemblatt and Resemblal, J. Am. Chem. Soc., 75, 4607 (1953).

XXXVIII is oxidized with excess peracetic acid to the diketone XL and to XLI in addition to the normal product XXXIX.<sup>28</sup> The rearrangement of the double bond from the  $\beta,\gamma$  to the  $\alpha,\beta$  position resembles that observed in other oxidations of  $\Delta^5$ -3-hydroxy steroids.<sup>106</sup> The oxidation of allo-

pregnan-20-one with persulfuric acid gives, in addition to the normal product and rostan-17 $\beta$ -ol, a significant yield of allopregnan-21-ol-20-one.<sup>47</sup> This arises from the action of the peracid on the enolic form of the C–20 keto group.<sup>18</sup>

## SELECTION OF EXPERIMENTAL CONDITIONS

Peroxides. Hydrogen peroxide, permono- and perdi-sulfuric acid, peracetic acid, perbenzoic acid, and monoperphthalic acid have all been used as reagents in the Baeyer-Villiger reaction. Although there is little precise information on the relative efficiencies of these peroxides, there is sufficient evidence to permit some general conclusions.

Hydrogen peroxide in dilute acid or in neutral solution sometimes converts carbonyl compounds to normal Baeyer-Villiger oxidation products, but more frequently hydroxylydroperoxides and their condensation products are formed. The simple and condensed peroxides XLII-XLV are produced by the action of hydrogen peroxide in diethyl ether on cyclohexanone. 107, 15 Similar compounds are formed from aliphatic aldehydes. 11

<sup>106</sup> Djerassi, Org. Reactions, 6, 212 (1951).

<sup>107</sup> Milas and Panagiotakos, J. Am. Chem. Soc., 61, 2430 (1939).

and fluorenone<sup>14</sup> under these conditions, although normal Bacyer-Villiger oxidation products are obtained without difficulty when peracids are used.

From these observations and the fact that the peroxides of cyclohexanone, fluorenone, and aliphatic aldehydes are converted by heating or by treatment with acids to the Baeyer-Villiger reaction products, it appears that hydrogen peroxide in ether or dilute acid is less effective since it does not favor the dissociation and rearrangement steps postulated for the Baeyer-Villiger reaction (p. 75).

In the related rearrangement of esters of the hydroperoxide formed from decahydronaphthalene (XLVI),<sup>2</sup> the dissociation step is influenced both by hydrogen-ion catalysis and by the nature of the acyl group RCO. The

acetate and benzoate rearrange readily on warming. The p-nitrobenzoate rearranges more readily than the benzoate, and all attempts to prepare the trichloracetate lead to the rearrangement product. By analogy, it may be expected that the Baeyer-Villiger reaction is favored by conditions leading to the formation of peroxide esters of relatively strong acids. There is little evidence on this point, but the fact that the organic peracids

have proved more generally useful than hydrogen peroxide is in agreement with this view. The more limited applicability of the persulfuric acids is to be attributed in part to the fact that their use in aqueous solution favors the formation of peroxides. Though persulfuric acids and their salts have been used successfully in non-aqueous media, organic peracids are more convenient.

Hydrogen peroxide in alkaline solution differs in reactivity from other Baeyer-Villiger reagents. In the Dakin reaction and the cleavage of  $\alpha$ -diketones, alkaline conditions are to be preferred. With  $\alpha,\beta$ -unsaturated ketones, however, these conditions lead exclusively to epoxyketones rather than Baeyer-Villiger reaction products. There has been a useful study of the kinetic course of the oxidation of mesityl oxide and of ethylideneacetone by hydrogen peroxide in an alkaline medium. 107a It would be desirable to obtain further information on the course and kinetics of reactions involving alkaline hydrogen peroxide.

In all peroxide oxidations of new compounds the possibility of reactions occurring with explosive violence must be considered. Trial experiments should be carried out using small quantities of material. Large excesses of reagents should be avoided, and if significant quantities of unconsumed peroxides remain at the end of the reaction they should be destroyed by reducing agents such as sodium bisulfite or ferrous sulfate before isolation of the products is attempted.

It is generally possible to follow the course of the Baeyer-Villiger reaction by estimating the active oxygen at intervals. Blank determinations should be carried out, particularly when long reaction times are involved, as the reagents may decompose under the conditions of the experiment. Information on conditions influencing the stability of peroxides is included in reviews on the general properties of hydrogen peroxide<sup>108–110</sup> and peracids.<sup>99</sup> In addition to temperature and pH, such factors as intensity of illumination, solvent polarity, and trace-metal impurities may play an important role.<sup>111–113</sup>

The following procedures are convenient for the preparation of the peroxides used in the Baeyer-Villiger reaction. Further information on methods of preparation of organic peracids is included in reviews, 95, 92, 114, and also procedures for the analysis of peroxides have been summarized, 115

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107a Bunton and Minkoff, J. Chem. Soc., 1949, 665.
108 Shanley and Greenspan, Ind. Eng. Chem., 39, 1536 (1947).
109 Medard, Compt. rend., 222, 1491 (1946).
110 Schumb, Ind. Eng. Chem., 41, 992 (1949).
111 Böeseken and Blumberger, Rec. trav. chim., 44, 90 (1925).
112 Calderwood and Lane, J. Phys. Chem., 45, 108 (1941).
113 Meerwein, Ogait, Prang, and Scrini, J. prakt. Chem., 113, 9 (1926).
114 Criegee, Fortschr. chem. Forsch., 1, 508 (1950).
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<sup>115</sup> Swern, Org. Reactions, 7, 392 (1953).

Hydrogen Peroxide. In alkaline solution, hydrogen peroxide decomposes relatively rapidly and is particularly sensitive to impurities. <sup>108</sup> These facts must be taken into consideration to ensure that a sufficient excess of reagent is available. The majority of Baeyer-Villiger oxidations involving alkaline hydrogen peroxide employ dilnte sodium hydroxide in slight excess of the amount required to keep the reactants and products in solution. Ammonium hydroxide <sup>52</sup> and potassium bicarbonate <sup>68</sup> have also been used, and pyridine has been added in reactions in which the sodium salt of the starting material is relatively insoluble in water. <sup>79, 94</sup>

Hydrogen peroxide in ether is conveniently prepared by shaking 50 g. of 30% hydrogen peroxide with five 100-ml. portions of diethyl ether. The ether extract is dried first with sodium sulfate and then with calcium chloride. It contains approximately 2% hydrogen peroxide. A more concentrated solution (4-6%) may be obtained by evaporation of ether from the dilute solution at room temperature under reduced pressure. 92 The concentration of hydrogen peroxide may be determined iodimetrically. Ceric sulfate is used for the titration of hydrogen peroxide when aldehydes are present. 86, 116

Hydrogen peroxide has also been used in acetone, 95 in formic acidchloroform, 117 and in acetic acid. 118 It has been shown in the oxidation of androsterone acetate that a dilute solution of peracetic acid in glacial acetic acid is preferable to hydrogen peroxide in acetic acid. 119

Persulfuric Acid. Baeyer and Villiger's "dry reagent" is prepared by mixing 10 g. of potassium persulfate with 11 g. of concentrated sulfuric acid in a mortar, adding 30 g. of potassium sulfate, and grinding the mixture to a fine powder. This reagent is stable in the absence of moisture.

Oxidations have been carried out using suspensions of the dry reagent<sup>1</sup> or solutions of persulfuric acid in glacial acetic acid,<sup>47</sup> in concentrated and dilute sulfuric acid, in petroleum ether,<sup>34</sup> and in ethanol-sulfuric acid.<sup>35</sup> Methods for the estimation of permono- and perdi-sulfuric acid have been described.<sup>120</sup>, <sup>121</sup>

Perbenzoic Acid. Details of the preparation of this acid are given in Organic Reactions.<sup>122</sup> A product of 99.7% purity is prepared by vacuum sublimation of crude material at 40°. <sup>123</sup>

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    Willard and Young, J. Am. Chem. Soc., 55, 3260 (1933).
    Prelog and Kocor, Helv. Chim. Acta, 31, 237 (1948).
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<sup>118</sup> Mannich, Ber., 74, 1007 (1941).

<sup>119</sup> Levy and Jacobsen, J. Biol. Chem., 171, 71 (1947).

<sup>120</sup> D'Ans and Friederich, Ber., 43, 1880 (1910).

<sup>121</sup> Rius and Zulueta, Anales real soc. españ. fts. y quim., 44B, 923 (1948) [C. A., 43, 2121 [1949]].

<sup>122</sup> Swern, Org. Reactions, 7, 394 (1953).

<sup>123</sup> D'Ans, Mattner, and Busse, Angew. Chem., 65, 57 (1953).

a typical example, benzophenone is oxidized by peracetic acid in glacial acetic acid to phenyl acetate in 44% yield in one hundred and ninety-two hours, but when concentrated sulfuric acid (25%) is added 82% conversion occurs in thirty minutes.<sup>4</sup>

The oxidation of carbonyl compounds with peroxides in the presence of metal catalysts<sup>132</sup>. <sup>133</sup> does not appear to follow the same course as the Baeyer-Villiger reaction.

Temperature and Time. A wide range of temperatures has been employed in Baeyer-Villiger oxidations. In some earlier applications of the reaction the carbonyl compounds were heated under reflux with peroxides in relatively high-boiling solvents. This is not to be recommended as a general procedure. Temperatures above 45° normally lead to excessive decomposition of peroxides, and under such conditions a large excess of reagent is required to replace the loss and may lead to oxidation of the normal products. There are exceptional cases involving the oxidation of aromatic aldehydes and ketones in which higher reaction temperatures have been used successfully, but in these oxidations short reaction times are involved.<sup>48, 94</sup> The reaction is normally carried out at a temperature of 10–40°. Lower temperatures may lead to excessively long reaction times and to reduced yields.<sup>35</sup>

When oxidations are carried out with organic peracids or hydrogen peroxide in neutral media, reaction times may vary from several hours to several weeks, according to the molecular species. As a typical example, oxidation of 3-ketosteroids with perbenzoic acid in chloroform is complete in sixteen hours at 16°, although under the same conditions 20-ketosteroids require seven to ten days for cleavage.<sup>27</sup>

In general, relatively short reaction times are required when oxidations are carried out in alkaline or strongly acidic media.

## EXPERIMENTAL PROCEDURES

The following examples illustrate typical procedures for the Baeyer-Villiger reaction.

Catechol (Dakin modification using hydrogen peroxide and sodium hydroxide solution). Detailed directions for the preparation of catechol from salicylaldehyde (69-73%)<sup>134</sup> and for a similar preparation of 3-methoxycatechol<sup>135</sup> are given in *Organic Syntheses*.

3,4-Dihydroxyphenanthrene (Dakin modification using alkaline hydrogen peroxide and pyridine). A solution of 1.11 g. of 3-hydroxy-4-formylphenanthrene (5 millimoles) in 10 ml. of pyridine is placed in a

<sup>133</sup> Treibs, Ber., 72, 1194 (1939).

<sup>133</sup> Milas, J. Am. Chem. Soc., 59, 2342 (1937).

Dakin, Org. Syntheses, Coll. Vol. 1, 149, 2nd ed., 1941.
 Surrey, Org. Syntheses, 28, 90 (1946).

25-ml. flask equipped with a dropping funnel and an exit tube. After the air has been displaced with hydrogen, 0.55 ml. of 30.8% hydrogen peroxide (50 millimoles) and 0.45 ml. of 12.5 N potassium hydroxide (5.6 millimoles) are added. The addition of potassium hydroxide causes a considerable rise in temperature. The solution is allowed to boil for a few seconds. It is then cooled, acidified with excess hydrochloric acid, and extracted with diethyl ether. The ether solution is washed with dilute hydrochloric acid to remove pyridine, dried, and evaporated. The crude residuc (1.05 g.) is recrystallized from benzene and petroleum ether to yield 0.83 g. (80%) of pure 3,4-dihydroxyphenanthrene, m.p. 142–3°.

Phenyl p-Nitrobenzoate (Oxidation of a diaryl ketone using peracetic acid with sulfuric acid as catalyst).<sup>4</sup> A solution of 4.54 g. of p-nitrobenzophenone (20 millimoles) in a mixture of 50 ml. of glacial acetic acid and 30 ml. of concentrated sulfuric acid is treated with external cooling with 8 ml. of 40% peracetic acid (40 millimoles). After thirty minutes at room temperature the mixture is neutralized with sodium carbonate solution and extracted with diethyl ether. The dried ether extract yields on evaporation 4.6 g. (95%) of phenyl p-nitrobenzoate, m.p. 128-130°.

Etiocholan-3α,12α,17β-triol (Oxidation of a 20-keto steroid using perbenzoic acid with sulfuric acid as catalyst).28 Ninety grams of 3a,12a-diacetoxypregnan-20-one (0.22 mole) and 44 ml. of a 10% solution of sulfuric acid in glacial acetic acid are added separately with external cooling to 440 ml. of a chloroform solution containing 68.6 g. (0.49 mole) of perbenzoic acid. The solution is allowed to stand in the dark at room temperature for ten days. After dilution with diethyl ether, the mixture is washed in turn with water, dilute sodium carbonate solution, and water. The organic layer is dried, and the solvent is evaporated. The residue is saponified by boiling for one hour with a solution of 60 g. of sodium hydroxide in 850 ml. of methanol and 50 ml. of water. After much of the methanol has been removed by distillation under reduced pressure, sufficient ether is added to keep the product in solution. The ether solution is washed with water until neutral, dried, concentrated to 600 ml., and cooled to -10° to precipitate 46.3 g. of etiocholan-3α,12α,17β-triol, m.p. 231-232°. Treatment of the concentrated mother liquor with Girard's Reagent P furnishes an additional 0.73 g. of the triol and 6.17 g. of starting material. The total yield of triol is 71%.

Diphenic Acid (Cleavage of an α-diketone using alkaline hydrogen peroxide). A suspension of 1 g. of 9,10-phenanthraquinone (4.8 millimoles) in 20 ml. of 5% aqueous sodium hydroxide is mixed with 2.5 ml. of 27% hydrogen peroxide (19 millimoles) and allowed to stand with

<sup>136</sup> C. H. Hassall, unpublished observations.

occasional stirring at 30°. Further additions of 2.5 ml. of 27% hydrogen peroxide are made after six hours and again after an additional twelve hours. After a total of forty-eight hours the mixture is filtered from a trace of insoluble material and acidified. The precipitate of pure diphenic acid formed is collected on a filter, washed with water, and dried; the yield is 1.09 g. (94%), m.p., 229-230°.\*

2-Acetoxyindan-1,3-dione (Selective oxidation of a triketomethane derivative using hydrogen peroxide in ether). A solution containing 1 g. of 2-acetylindan-1,3-dione (5.3 millimoles) in 80 ml. of diethyl ether is treated with 12 ml. (18 millimoles) of 5% hydrogen peroxide in ether and allowed to stand in a closed flask at 15°. After twenty-one days the ether is evaporated. The residue is triturated with 3 ml. of water, filtered, and extracted with chloroform. The ehloroform extract is filtered from a trace of phthalic acid and evaporated. The residue is crystallized twice from ethyl acetate-petroleum ether (40-60°) to give 0.70 g. (64%) of 2-acetoxyindan-1,3-dione, m.p. 96°.

Lactone  $C_{21}H_{32}O_4$  from Isoandrosterone Acetate (Oxidation of a 17-keto steroid using peracetic acid with p-toluenesulfonic acid as catalyst).<sup>119</sup> A solution of 0.274 g. of isoandrosterone acetate (0.83 millimole) in 2 ml. of glacial acetic acid, 5 ml. of 9.5% peracetic acid in acetic acid (6.75 millimoles), and 25 mg. of p-toluenesulfonic acid are mixed and allowed to stand for twenty-three hours at 35° in the dark. The mixture is then treated with a large excess of water which precipitates 0.252 g. (88° o) of the crude lactone, m.p. 156-158.5°. This product is converted by one crystallization from benzene-neohexane to the pure lactone,  $C_{21}H_{32}O_4$ , m.p. 158-159.5°.

# Baryer-Villiger Oxidation of Saturated Aliphatic Ketones

	Carbonyl Compound	Reagent.	Product	Yleld, %	Reference
0,11,0	Acetone	11,50,	Aectone peroxide	99	138, 139, 140, 64
		11.0. 11.80.	Acetone peroxide, hydroxyacetone	ĺ	21
0 11 3	Butanone	11.0. 11.80.	Butanone peroxide, 3-hydroxybutanone	I	21, 140
	Acetylevelonronano	C.11.CO.11	No reaction	I	141, 23
C. II. C	3-Pentanone	11,0,11,50,	3-Pentanone peroxide, 2-hydroxypentan-3-one	ı	21
00110	Acetelevelohutane	c.ii.co.ii	Cyclobutyl acetate	58	23
0,11,0	Veetvlevelonentang	Call Co. H	Cyclopentyl acetate	10	23
0,11,0	cis-1-Acetyl-2-methyleyelopentane	C'II CO'II	cis-2-Methyleyclopentyl acctate	00	7
	trans-1-Acetyl-2-methylevelopentane	cilicoin	trans-2-Methyleyelopentyl acetate	64	2
	Arctyleyelohexane	c,in,co,in	Cyclohexyl acetate	67	141, 23
0.11.0	2.Octanone	11,0, HF	n-Hexyl acetato	51	20
0,11,5	cis-1-Acetyl-2-methyleyclohexane	c,ir,co,ir	cis-2-Methyleyelohexyl neetate	03	2
-	trans-1-Acetyl-2-methyleyelolickane	c,n,co,n	trans-2-Methyleyelohexyl acetate	55	2
	Acetyleyeloheptane	c,11,co,11	Cycloheptyl acetate	60	23
C,611,20	3-Phenylbutan-2-one	Canscoan	Phenylmethylearblnyl acetate	87	30
0,11,0	circis. Acetyldecally dronaphthalene	C <sub>0</sub> 11 <sub>5</sub> CO <sub>3</sub> 11	cis-cis-Decallydro-2-naplithol	65	35
0,11,10	Allopregnan-20-one	K,S,O,, CH,CO,H, H,SO,	Allopregnan-21-ol-21-one acetate, androstan-17 $\beta$ -olf	30–35	47
C1111102	Δ³.Pregnen•3β·01•20·0ne	C <sub>6</sub> 11 <sub>5</sub> CO <sub>3</sub> 11	Testosterone acetate, progesterone, $\Delta^5$ -androsten-38.178-diol 12-monometate	!	28
$C_{23}\Pi_{34}O_{3}$	As-Pregnen-3/9-01-20-one acctate	Monoperphthalle aeld, CHCl3;	Δ5-Androsten-3β,17β-diol	63	28, 47
:		C,11,CO,11, CHC1, H,SO,	Δ5-Androsten-3β,17β-dlol	09	80
C23113104		Confcoan	Etiocholan-3a,17\(\beta\)-diol-11-one diacetate \(\pi\)	85	27
C231135O3		C,H,CO,II	Androstan-3\(\theta\),17\(\theta\)-diol\(\theta\)	က	40
	Allopregnan-32-01-20-one acetate	K2S2O8, CH3CO211, H3SO1	Androstan-3a,17\(\theta\)-diol diacetate\(\theta\)	I	142
	Pregnan-3x-ol-20-one acetate	$C_6\Pi_8CO_3\Pi$	Etiocholan-3 $\alpha$ ,17 $\beta$ -diol diacetate	55	31, 47
;		Calls Co311	Etlocholan-3x,17x-diol diacetate	53	31
C <sub>23</sub> 1139O <sub>3</sub>		Callscoall, Chicle, Ilesoas	Etlocholan- $3\alpha$ , $12\alpha$ , $17\beta$ -friol	2.2	28, 27
C24 II34O4	Pregnan-3x-ol-11,20-dlone benzoate	C <sub>6</sub> 11 <sub>3</sub> CO <sub>3</sub> 11	Etiocholan-3a,17\(\beta\)-I1-one 3-benzonte 17-acetate †	18	27
Veter D	Volst Beforences 199 164 can Make I and				

Note: References 138-164 are listed on p. 106.

† The configuration at C-17 assigned by the author has been changed. The correction follows from the unequivocal evidence, only available after the completion of . Where CH3CO3H is indicated, acetic acid is always present; where H3SO3 is shown, sulfurle acid is present; where C3H3CO3H is shown, chloroform is present.

the investigation, that the Bacyer-Villiger reaction occurs with retention of configuration.  $^{*}$  A catalytic amount of p-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>SO<sub>5</sub>H was added. § Catalytic amount,

## ORGANIC REACTIONS

TABLE II

## BABYER-VILLIGER OXIDATION OF ALICYCLIC KETONES

		Rengent	Language Control of the Control of t		-
	Carbonyl Compound			20	#
0°11°0 0°11°0	Cyclobutanone Cyclopentanone	C <sub>6</sub> H <sub>5</sub> CO <sub>3</sub> H H <sub>2</sub> O <sub>2</sub> , NaOH H <sub>2</sub> O <sub>2</sub> , HF K <sub>5</sub> S <sub>2</sub> O <sub>6</sub> , H <sub>5</sub> SO <sub>1</sub> , C <sub>2</sub> H <sub>5</sub> OH	Butyrolactone 5-Hydroxyvaleric acid Jactone Polyesters of 5-Hydroxyvaleric acid Ethyl 5-Hydroxyvalerate 11-11-11-11-11-11-11-11-11-11-11-11-11-	81 86-89 70 87	37, 36 20 113, 35
0.4.0	Cyclolexanone	C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> H H <sub>2</sub> O <sub>2</sub> , HNO <sub>3</sub> H <sub>2</sub> O <sub>2</sub> , HF	J-11) utray mirror Cyclopentainone peroxide 6-Hydroxycaprole neld lactone, polycaters of 6-hydroxycaprole	8, 81	± 0;
011119		H <sub>2</sub> SO <sub>3</sub> u co C.H.OH	acid Polyesters of G-hydroxycaprolc acid Ethyl G-hydroxycaproate	1 = 5	110, 69 35
		N-2-Or 1120-1 C113 11302 NaOH C4113C0311	6-Hydroxycaprole acld 6-Hydroxycaprole acld lactone	271	5, 114 133
C,II,2O	3-Methylcyclohexanone Cycloheptanone	K <sub>2</sub> 'S <sub>2</sub> O <sub>9</sub> , II <sub>2</sub> SO <sub>4</sub> K <sub>3</sub> S <sub>2</sub> O <sub>8</sub> , II <sub>2</sub> SO <sub>4</sub> , C <sub>2</sub> II <sub>3</sub> OH C <sub>2</sub> II,CO <sub>4</sub> H	3-Methyrythomestation of the Ethyl 7-hydroxyleptanoate 7-Hydroxyenantile acid lactone	55 55	35, 138 5
C <sub>8</sub> H <sub>11</sub> O	Cyclosetanone a-Tetralone	ี่ กรูชง	s.Hydroxycapryne acid daetone  -11ydroxy-1-(0-hydroxyphenyl)-   butyrle acid lactone	; I	211
011.01	Tolores Marie Mari	$II_2 SO_3$	Campholide	위 2	
C10H160	p-Menthan-2-one	If <sub>2</sub> SO <sub>3</sub>	hetone hetone a nedene	ÿ	110, 138
	Menthone	$\Pi_2 SO_3$	acld Inctone	:	12
C13H240 C141I260	Cyclotrideeanone Cyclotetradeeanone	11,50, 11,50, CH,CO,II	13-Hydroxytrhiceanoic acid larfoue H-Hydroxymyristic acid lactone 15-Hydroxypentadecanoic acid	35.71	# # #
0,511,51	Cyclopentatecanone ( pourone)	II,02, II,304	lactone Cyclopentadecanone peroxide, 15-hydroxypentadecanole acid	1	146
C,4H30	Cyclohexadecanone	M.280, M.890,	jactone 16.Mydrasynalnille acid lactone 17.Nydroxymargarie acid lactone	8.5	31

C18 H210 GC18 H300	Extrone Androstan-3-one	H, O2, NaOH C <sub>6</sub> H, CO3H	Lactone $C_{19}H_{22}O_{3}$ Lactone $C_{19}H_{30}O_{2}$	10	36
C <sub>10</sub> 11 <sub>30</sub> 0 <sub>2</sub> C <sub>20</sub> 11 <sub>20</sub> 0 <sub>3</sub>	Androstan-3-one-17\$-ol Bquilenin acetato (±}-Isocquilenin acetato	0=( 0 <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> H CH <sub>3</sub> CO <sub>3</sub> H† CH <sub>3</sub> CO <sub>3</sub> H†	H Lactone $G_{19}H_{10}O_3$ Acetate of lactone $G_{18}H_{19}O_3$ Acetate of lactone $G_{18}H_{19}O_3$	32 69 69	43 147 46
C <sub>0</sub> 11103 C <sub>11</sub> 11303 C <sub>11</sub> 113103 C <sub>12</sub> 1131100 C <sub>13</sub> 1131100 C <sub>13</sub> 1131003 C <sub>2</sub> 1111003 C <sub>2</sub> 11111003 C <sub>2</sub> 11111003 C <sub>2</sub> 11111003 C <sub>2</sub> 11111003	Estrone acetate  As-Pregnen-3\theta-01-20-one Andivorterone acetate Isoandrosterone acetate 4-Bronno-12x-acetoxypregnan-3.20-dione A1-3-Ketocholonic acid methyl ester 3-Keto-lollanic acid methyl ester Bitocholan-17\theta-03-one benzoate 3-Keto-12\theta-acetoxycholanic acid methyl ester Cholestandione Coprostan-3-one Collocatan-3-one 7-Ketocholestan-3\theta-0i	CII  H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> II  H <sub>2</sub> → C <sub>4</sub> H <sub>3</sub> CO <sub>3</sub> II + Zn  CH <sub>3</sub> CO <sub>3</sub> II + C <sub>4</sub> H <sub>3</sub> CO <sub>3</sub> II +  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + pyrldine  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + pyrldine  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II  C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II + C <sub>6</sub> H <sub>3</sub> CO <sub>3</sub> II	CII <sub>3</sub> CO <sub>2</sub> Acetate of lactone C <sub>18</sub> H <sub>22</sub> O <sub>3</sub> Lactone C <sub>21</sub> H <sub>30</sub> O <sub>3</sub> Acetate of lactone C <sub>19</sub> H <sub>30</sub> O <sub>3</sub> Acetate of lactone C <sub>19</sub> H <sub>30</sub> O <sub>3</sub> Acetate of lactone C <sub>19</sub> H <sub>30</sub> O <sub>3</sub> Lactone C <sub>21</sub> H <sub>30</sub> O <sub>4</sub> Lactone C <sub>22</sub> H <sub>31</sub> O <sub>4</sub> Lactone C <sub>27</sub> H <sub>31</sub> O <sub>3</sub>	67-63 70 70 89-92 68 68 95 14 80 80 87	45 03 1110 119 119 63 40 41 40 40, 39 40, 49
C29H48O3 7 Note: Refer	Cr. H48O3 7-Ketocholestan-38-ol acetate (benzoate or pivalate) C <sub>6</sub> H <sub>5</sub> CO <sub>3</sub> H  Note: References 138-164 are listed on p. 106.  Where CH <sub>3</sub> CO <sub>3</sub> H Is indicated, acetic acid is always present: whose 17 co. 3. 11.00	C <sub>6</sub> H <sub>5</sub> CO <sub>5</sub> H	Derivatives of lactone C <sub>27</sub> H <sub>46</sub> O <sub>3</sub>	86-100	<del>1</del>

" near ClisColi is indicated, acetic acid is always present; where II\_SO<sub>2</sub> is shown, sulfuric acid is present; where C<sub>6</sub>H<sub>5</sub>CO<sub>3</sub>H is shown, chloroform is present.

A catalytle amount of p-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H was added.

		TABLE III	III	Olypycoanurit	KETONES
	ATTRIBUTED AROMATIC, ALICYCLIC AROMATIC, ANOMATIC, AND HELPINOCLOSES	IOMATIC, ALICYC	ILIC AROMATIC, AROMATIC, AND	HEIRINGTON	
BAEYEI	R-VILIGER OXIDATION OF THE			Yield, %	Reference
1		Reagent	Product		-
	Carbonyl Compound			57	10
1		H.00.H	p-Chlorophenyl ncetato	33	48,4
25	m. Chloroacetophenone	11.00.11	Phenyl ncetata	63	111
2011	Aeetophenono	C.11.00,11	Phenyl ncetate	1	123
C81187		II O. WII.	Catechol	i	Ç,
0.11.0	o-Hydroxyaeetophenono	11.02, NII3	No reaction	10-20	: 2
50 81150	m.Hydroxyacetophenone	11.0. NII,	Hydroqulnone	1	22
	n-IIydroxyacetophenone	11.0. NII.	Hydroxyhydroquinone	1	e1 C2
0 11 0	2, 4. Dihydroxyaeetophenono	IIN O	Hydroxyhydrodulnone	93	18
0811803	2.5.Dihydroxyacetophenone	CILCOTI	4-Methoxy-f-chioropheny accurre-	Trace	
C.11.0.Cl	2-Methoxy-4-chloroacetophenone	7 0 5 10	5-chlorogualacol	55	2
201.60		C.11.CO.11	p.Cresyl acetale	£7.	111
C.11.0	p-Methylaectophenone	C.11,CO.11	Phenyl proplonate	1	72
-0160	Propiophenone	H.O. NII.	Hydroquinone	ì	5
0,11,0	p-IIydroxyproplophenone	CH-CO-11	Gunfacol	21	10
2-01-160	o-Methoxyaectophenone	C.H.CO.H	m-Methaxyphenyl acetato	99	10, 14, 90,
	m-Methoxyacetophenone	C. II. CO. II	p-Methoxyphenyl acctate		91
	p-Methoxyacetophenone	-F S		1	150
		If.0., XII.	1.2-Dillydroxy-1-methoxybenzene	0#	01
C.H.,O,		C. 11. CO. 11	flydroquinone diacetate	9	7.
Colling		C.11.CO.11	p-Acetaminophenyl acetale	2 1	<del>2</del> 2
C,0H,1NO2		CIT.CO.11	2,4-Dimethoxyphenol	1	<u>8</u> ;
C,011,203		CIL.CO.II	2,5-Dimethoxyphenyl acetate	00	151
!	2,5-Dimethoxyacetophenone o 4-Dinydroxy-3,5-dimethylaeetophenone (clavatol)	II.o., Nuoli	3-IIydroxy-2,6-dimethylbenzoqumone	1	
	1. C				

97 48 48 48 14	4 4 4 4 4	4, 131 140, 4 4 4 4	48 162 4 4 4 152	152 152 152 4
1         802	96  54, 82 60 77	95 Quantifative 38 6, 33, 5, 5		11112
No product isolated 2.4.5-Trimethoxyphenyl acetate 2.3,4-Trimethoxyphenyl acetate 4.6-Dimethoxyresoreinol diacetate 2-Hydroxybiphenyl-2-carboxylic acid lactone Plucronone peroxyli	2-Hydroxybiphenyl-2-carboxyllc aeld lactone No reaction p-Nitrophenol, p-nitrobenzoic acid Phenyl p-bromobenzoate Phenyl p-chlorobenzoate, phenol, p-chloro-	Denote actual Phenyl p-nitrobenzoate Phenyl p-nitrobenzoate Phenyl p-aminobenzoate Cyclohexanol, benzole acid, phenol, hexa- hydrobenzoic acid Chalcher i banzole acid, chantl becohedrate	45.6.Trimethoxyresorelnol diacetate 2,4.5.Trimethoxyresorelnol diacetate o-Aminobenzophenone p-Cresyl benzoate p-Methyr-o'-aminobenzophenone o-Methyr-o'-aminobenzophenone p-Methyr-o'-aminobenzophenone	o-Methoxy-o'-aminobenzophemene rTolnic netd F-Methoxy-o'-aminobenzophemene Benrok ackl
C <sub>4</sub> H <sub>5</sub> CO <sub>3</sub> H CH <sub>3</sub> CO <sub>3</sub> H• CH <sub>3</sub> CO <sub>3</sub> H• CH <sub>3</sub> CO <sub>3</sub> H• CH <sub>3</sub> CO <sub>3</sub> H· CH <sub>3</sub> CO <sub>3</sub> H· H <sub>2</sub> SO <sub>4</sub> H <sub>2</sub> O <sub>2</sub> , (C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> O	H <sub>2</sub> SO <sub>5</sub> , (CH <sub>3</sub> CO) <sub>2</sub> O CH <sub>3</sub> CO <sub>3</sub> H, H <sub>2</sub> SO <sub>4</sub> CH <sub>3</sub> CO <sub>3</sub> H, H <sub>2</sub> SO <sub>4</sub> CH <sub>3</sub> CO <sub>3</sub> H, H <sub>2</sub> SO <sub>4</sub> CH <sub>3</sub> CO <sub>2</sub> H, H <sub>2</sub> SO <sub>4</sub>	CH,CO,H, H,SO, H,SO, (CH,CO),O CH,CO,H, H,SO, CH,CO,H	CH <sub>3</sub> CO <sub>3</sub> L <sub>3</sub> CH <sub>3</sub> CO <sub>3</sub> L <sub>4</sub> CH <sub>3</sub> CO <sub>3</sub> L <sub>4</sub> CO <sub>3</sub> L <sub>4</sub> CO <sub>3</sub> L <sub>4</sub> CH <sub>3</sub> CO <sub>4</sub> L <sub>4</sub> CO <sub>4</sub> CO <sub>4</sub> L <sub>4</sub> CO <sub>4</sub> CO <sub>4</sub> L <sub>4</sub> CO	Hop. Naoh Hop. Naoh Hiop. Naoh Hiop. Naoh
Acctomestyteoc 2,4,5-Trimethoxyacetophenone 2,3,1-Trimethoxyacetophenone 1,3-Diacetyl-4,6-dimethoxybenzene Fluorenone	o, p'-Dinitrobenzophenonc p., p'Dinitrobenzophenonc p-Bromobenzophenene p-Chlorobenzophenonc	p-Nitrobenzophenone Benzophenone p-Aminebenzophenone Phenyi eyelohexyi ketone	1.3-Dlacetyl-4.5.6-trlmethoxybenzene 1.3-Dlacetyl-2.4.5-trlmethoxybenzene 3-Phenyldloxindole p-Methylbenzophenone p-Methylbenzophenone 3-(a-Tolylyldloxthidole 3-(a-Tolylyl)dloxthidole 3-(a-Tolylyloxindole	C <sub>1</sub> H <sub>12</sub> NO <sub>2</sub> 5-(e-Methoxyphemyl)dioxindolo 3-(m-Methoxyphemyl)dioxindole 5-(p-Methoxyphemyl)dioxindole 5-(p-Methoxyphemyl)dioxindole 7-(p-Methoxyphemyl)dioxindole N-N-N-Reitzenson 188-484 are Beart on p. 10M.  - A cotale its amount of 2-(Pigligh Reitzen and M.).
0"1"" 0"1"" 0"1"" 0""" 0"""	C <sub>13</sub> 11 <sub>8</sub> N <sub>2</sub> O <sub>5</sub> C <sub>13</sub> 11 <sub>9</sub> BrO C <sub>13</sub> 11 <sub>8</sub> ClO	C13H3NO3 C13H100 C13H12NO C13H12N	C11H18O2 C14H11O2 C14H1O C14H1O2 C11H13O2	CBHBNO

## TABLE IV

Babyer-Villiger Oxidation of  $\alpha, \beta.$  Unsaturated Carronyl

eld, % Reference	101	153, 53 63, 54, 153 63, 56, 153 57 77 77 77 77 77 77 77 77 77 77 63 63 65 148	
Yleld, %	63-6	86   15   88   12   88   98   98   98   98   98   98   9	
Product		cia-Eighyther course 1,1-Dimethyl-2-actylethylene oxide a-Naphthoullone oxide Bnol acetate of pienylaceladehyde Bnol acetate of pienylaceladehyde Bnol acetate of methylene oxide 2-Methyl-1,4-naphthoriulnone oxide 2-Methyl-1,4-naphthoriulnone oxide 2-Methyl-1,4-naphthoriulnone oxide Enol proplonate of pienylacetalidehyde Enol proplonate of pienylacetalidehyde (±)-11-Keto-16x,17a-rpoxy-21-norprograferone (10,11-Epoxylecandanthrone 10,11-Epoxylecandanthrone 10,11-Epoxylecandanthrone, benzolc acid 2-1)methylaminoanthronen, benzolc acid 2-1)methylaminoanthronen, benzolc acid 15,7-Epoxypregna-5-en-3p-ol-20-one are tate Methyl A'-11,12-epoxy-3-ketocholenate Lactone Czall <sub>11</sub> O <sub>2</sub>	
BABYER-VILLIGER OXLAND	Псаков	11,02, NaOH 11,02, NaOH 11,03, NaOH 11,03, NaOH 11,03, NaOH 12,03, NaOH 11,03, NaOH 12,03, NaOH 13,03, NaOH 13,03, NaOH 14,03, NaOH 15,03,	
BAEYER-VILLI	Carbonyl Compound	jjenzoquinono Mesityi oxido a.Anphthoquinono Benzalacetone Gitral 2.Methyi 4.4-naphthoquinono Methyi 4-methyistryi ketono Binyi stryi ketono Henzalanekophkonone 10-Benzalantistono 10-Benzalantistono 2.Dimethylamino-10-benzalantistono pregastra, 1, 4-dien-38-ol-20-one acetati Methyi A4-11-3-ketocholadienate A4-Cholesten-3-one	. 100 to 10to listed on D. 100.
		C <sub>0</sub> H <sub>1</sub> O <sub>2</sub> C <sub>0</sub> H <sub>1</sub> O <sub>2</sub> C <sub>0</sub> H <sub>1</sub> O <sub>3</sub> C <sub>10</sub> H <sub>1</sub> O <sub>3</sub> C <sub>10</sub> H <sub>10</sub> O C <sub>10</sub> H <sub>10</sub> O C <sub>11</sub> H <sub>12</sub> O C <sub>11</sub> H <sub>12</sub> O C <sub>11</sub> H <sub>12</sub> O C <sub>11</sub> H <sub>13</sub> O C <sub>11</sub> H <sub>13</sub> O C <sub>12</sub> H <sub>13</sub> O C <sub>21</sub> H <sub>10</sub> O	

Note: References 138-164 are listed on p. 106.

TABLE V
BAEYER-VILIGER OXIDATION OF POLYCARBONYL COMPOUNDS

c <sub>Q</sub> H <sub>Q</sub> O <sub>2</sub> Blacetyl Eurly pyrrate Perplithalic acid Acette neld Momethyle ster of acette-carbonic anhydride 24, Children 25, Tribrono-4-hydroxymuconolactone 17, Children 26, Children 26, Children 26, Children 27, Children 27		Carbonyl Compound	Reagent	Product	Yield, %	Reference
Blacety    Perplithalic acid   Acetle neld			a-Dikelones			
Tetrahlomore	C.H.O.	Biacetyl	Perplithalic acid	Acetic neid	či	67, 61
Tetrabiomo-o-benzoquinone   C <sub>0</sub> H <sub>1</sub> CO <sub>2</sub> H   2.3.5-Tribromo-4-bydroxymuconolactone   30	C.H.O.	Ethyl pyriivate	Perphthalle aeid	Monoethyl ester of acetie-carbonle anhydride	ı	8
Tetrachloro-o-benzoquinone   Perphthalic acid   2.3.5-Tichhoro-i-hydroxymuconolactone   4	C.Br.O.	Tetrabromo-o-benzoquinone	C, H, CO, H	2,3,5-Tribronio-4-hydroxymuconolaetone	30	17, 154
Perpithalic seld	C,C1,O,	Tetrachloro-o-benzoquinone	Perpithalic acid	2,3,5-Trichloro-4-hydroxymueonolaetone,	₩	155
Perpithhalic acid	7		•	tetraeliloroniueonie acid	31	
Hexane-3,4-dione         Perphthalle aedd         Prophthalle aedd         Prophthale aedd         Prophthale aedd         Prophthale aedd         P-Methylmuconic anhydride         —           P.Methylphenylglyoxalate         Perphthalia aedd         Prophthalia aedd         Prophthalia aedd         P-Mitophenyljacet or benzole-arbonic anhydride         —           P.Maphthoquinone         CH3,O2,H         O-Carboxyallocinnamic aeld         76           P.Maphthoquinone         CH3,O3,H         O-Carboxyallocinnamic aeld         22           P.Methoxy-1,2-naphthoquinone         CH3,O3,H         O-Carboxyallocinnamic aeld         22           P.Methoxy-1,2-naphthoquinone         CH3,O3,H         Prophthalia aeld         2-Carboxy-5-methoxyeinnamic aeld         23           Acanaphthaequinone         CH3,O3,H         1-Carboxy-5-methoxyeinnamic aeld         2-Carboxy-5-methoxyeinnamic aeld         2-Carboxy-6-methoxyeinnamic aeld         2-Carboxy-6-methoxyeinnamic aeld	C,H,O,	o-Benzoquinone	CII3CO3H	cis,cis-Mueonle acid	ı	19
p-Methylo-benzoquinone         Perpitthalic acid         p-Methylu-benzoquinone         Perpitthalic acid         Amonochyl ester of benzole-carbonic anhydride         22           Elhyl phenylgyoxalate         Frzilithalic acid         Monochyl ester of benzole-carbonic anhydride         —           1.2.4-Tilketo-3.3.5.5-tetramethyleyelopentane         In 20, Ma Oll         To carboxyallocinnamic acid         76           β-Naphthoquinone         CH <sub>3</sub> CO <sub>3</sub> H         Perpitthalic acid         -Carboxyallocinnamic acid         22           β-Naphthoquinone         CH <sub>3</sub> CO <sub>3</sub> H         Phthalic acid         -Carboxy-5-methoxycinnamic acid         22           β-Methoxy-1.2-naphthoquinone         CH <sub>3</sub> CO <sub>3</sub> H         Phthalic acid         Phthalic acid         2-Carboxy-5-methoxycinnamic acid         23           β-Methoxy-1.2-naphthoquinone         CH <sub>3</sub> CO <sub>3</sub> H         1-Carboxy-5-methoxycinnamic acid         2-Carboxy-5-methoxycinnamic acid         23           β-Bromolaccain         1-Carboxy-1.2-methoxycinnamic acid         1-Carboxy-1.2-methoxycinnamic acid         2-Carboxy-2.3.5-tricarboxycinnamic acid         2-Carboxy-2.3.5-tricarbo	C,H,O,	Hexane-3,4-dione	Perphthalle aeld	Propionic acid	1	67
Ethyl phenylglyoxalate	C,H,O,	p-Methyl-o-benzoqulnone	Perphthalle aeld	B-Methylmueonic aphydride	81	GS
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	C,H,O	Ethyl phenylglyoxalate	Perplthalle acld	Monoethyl ester of benzoic-earbonie anhydride	ı	æ
1,2,4-Trikcto-3,3,5,5-tetramethyleyelopentane   H <sub>2</sub> O <sub>2</sub>   Tetramethylacetonedicarboxylle neid   To   To   To   To   To   To   To   T	CH,NO	o-Nitrophenylpyruvic acid	п,0,, NаОП	o-Nitrophenylaectie aeld	99	59
β-Naphthoquinone         CH <sub>3</sub> CO <sub>3</sub> H         o-Carboxyalloeinnamic acid         76           G-McHoxy-1,2-naphthoquinone         CH <sub>3</sub> CO <sub>3</sub> H         o-Carboxyalloeinnamic acid         22           G-McHoxy-1,2-naphthoquinone         Perphthalic acid         2-Carboxy-5-methoxycinnamic acid         23           Acenaphthoquinone         CH <sub>3</sub> CO <sub>3</sub> H         2-Carboxy-5-methoxycinnamic acid         31           Acenaphthoquinone         H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> H         2-Carboxy-5-methoxycinnamic acid         31           Acenaphthenequinone         H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> H         2-Carboxy-5-methoxycinnamic acid         31           9.10-Phenaphtrenequinone         H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> H         2-4-Dinitrophenol         53           9.10-Phenaphtraquinone         H <sub>2</sub> O <sub>2</sub> , NaOH         Diplemic acid         Quantitative           9.10-Phenaphtraquinone         GH <sub>2</sub> O <sub>2</sub> H         2-4-Dinitrophenol         70           9.10-Phenaphtraquinone         GH <sub>2</sub> O <sub>2</sub> H         NaOH         Diplemic acid         Quantitative           9.10-Phenaphtraquinone         GH <sub>2</sub> O <sub>2</sub> H         NaOH         Benzole acid         Quantitative           9.10-Phenaphtraquinone         GH <sub>2</sub> O <sub>2</sub> H         NaOH         Benzole acid         Phenaphtralic           1.3-Diphenylpropane-1,2-dione         CH <sub>2</sub> O <sub>2</sub> H         NaOH         Anisic acid <td>C,H,2O,</td> <td>1,2,4-Trikcto-3,3,5,5-tetramethyleyelopentane</td> <td>H_0_</td> <td>Tetramethylacetonedicarboxylle neld</td> <td>Quantitative</td> <td>7.0</td>	C,H,2O,	1,2,4-Trikcto-3,3,5,5-tetramethyleyelopentane	H_0_	Tetramethylacetonedicarboxylle neld	Quantitative	7.0
Control of the cont	C10H6O2	$\theta$ -Naphthoquinone	сизсозн	o-Carboxyalloeinnamic aeid	202	61
6-Methoxy-1,2-naphthoquinone         CH3CO3H         Phthalic acid         2-Carboxy-5-methoxycinnamic acid         23           6-Methoxy-1,2-naphthoquinone         CH3CO3II         2-Carboxy-5-methoxycinnamic acid         23           Acenaphthenequinone         H3CO2, CH3CO2II         4-Ketoarboxy-1-methoxycinnamic acid         31           10 22'.4.4.7-Tetranitrobcnzil         H2O2, NAOII         2-1-Dinitrophenol         53           9,10-Phenanthraquinone         H2O2, NAOII         2,4-Dinitrophenol         9,4-Dinitrophenol           9,10-Phenanthraquinone         CH3CO2II         2,4-Dinitrophenol         9,4-Dinitrophenol           Benzil         CH3CO2II         2,4-Dinitrophenol         9,4-Dinitrophenol           Benzil         CH3CO2II         2,4-Dinitrophenol         9,4-Dinitrophenol           Benzil         CH3CO2II         Diphenic acid         Quantitative           Benzil         CH3CO2II         Benzole acid         70           H2O2, CH3CO2II         Benzole acid         70           H4O2, CH3CO2II         Anisic acid, benzole acid         77           Anisic acid         Anisic acid         Anisic acid         77           Anisic acid         Anisic acid         70           Berphthalic acid         Parkylacrylic acid         70			$c_{\rm eH_5}co_{ m JH}$	o-Carboxyallocinnamic anhydride	61	17
6-Methoxy-1,2-naplthoqulnone         Perphthalic acid         2-Carboxy-5-methoxyeinnanic acid         23           Acenaphtheacquinone         II <sub>2</sub> O <sub>2</sub> , CII <sub>2</sub> CO <sub>2</sub> II         +-Ketocarboxy-5-methoxyeinnanic acid         31           10. 2,2',4,4'-Tetranitrobenzil         II <sub>2</sub> O <sub>2</sub> , CII <sub>2</sub> CO <sub>2</sub> II         Naplitalic acid            10. 2,2',4,4'-Tetranitrobenzil         II <sub>2</sub> O <sub>2</sub> , NaOII         2,4-Dinitrophenol         53           10. Phenanthraquinone         CII <sub>2</sub> O <sub>2</sub> II         Diplicit acid         Quantitative           9,10-Phenanthraquinone         CII <sub>2</sub> O <sub>2</sub> II         NaOII         Diplicit acid         Quantitative           9,10-Phenanthraquinone         CII <sub>2</sub> O <sub>2</sub> II         NaOII         Diplicit acid         Quantitative           9,10-Phenanthraquinone         CII <sub>2</sub> O <sub>2</sub> II         NaOII         Diplicit acid         Quantitative           1,3-Diphenylpropane-1,2-dione         C <sub>2</sub> II <sub>2</sub> O <sub>2</sub> II         NaOII         Benzole acid         Park           p-Methoxybenzil         C <sub>2</sub> II <sub>3</sub> O <sub>2</sub> II         NaOII         Anisic acid, benzole acid         Park           p-Methoxybenzil         C <sub>2</sub> II <sub>3</sub> O <sub>2</sub> II         NaOII         Anisic acid, cluyl anisoate         770           p-Methoxybenzil         C <sub>2</sub> II <sub>3</sub> O <sub>2</sub> II         NaOII         Anisic acid         Park           p-Methoxybenzil<			сизсозн	Phthalic aeld	ı	156
Cli_3CO_1   Cli_3CO_2   Craboxy-5-methoxyelmanle acid   31	$c_{11}H_{8}O_{3}$	6-Methoxy-1,2-naphthoquinone	Perplithalic acid	2-Carboxy-5-methoxyeinnamic acid	133	59
F-Bromolaccaln	1		$CH_3CO_3II$	2-Carboxy-5-methoxyeinnamle acid	31	59
Acenaphthenequinone         CH <sub>3</sub> CO <sub>3</sub> H         Naphthalie acld         —           10 2,2',4,4'Tetranitrobenzil         H <sub>2</sub> O <sub>2</sub> , NaOII         2,4-Dinitrophenol         53           9,10-Phenanthraquinone         H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> II         2,4-Dinitrophenol         94         1           Benzil         H <sub>2</sub> O <sub>2</sub> , NaOII         Diplienic acld         70         94         1           Benzil         CH <sub>3</sub> O <sub>2</sub> , NaOII         Benzolc acld, cthyl benzoate         70         94         1           1,3-Diphenylptopane-1,2-dione         CH <sub>3</sub> O <sub>2</sub> H, NaOII         Benzolc acld, cthyl benzoate         83         83           1,3-Diphenylptopane-1,2-dione         C <sub>3</sub> H <sub>3</sub> O <sub>2</sub> H, NaOII         Benzolc acld, phenylacette acld         61         70           p-Methoxybenzil         C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> H, NaOII         Anisic acld, benzolc acld         779         779           Anisil         C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> H, NaOII         Anisic acld, benzolc acld         770         770           Anisil         C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> H, NaOII         Anisic acld, benzolc acld         770         770           Bricheneblacetyl         Perphthalle acld         2-Styrlacrylic anlydride         66         66           Bricheneces 138-104 are listed on p. 106.         2-Styrlacrylic anlydride         2-Styrlacrylic acld         2-Styrlacrylic an	$c_{12}H_5BrO_6$	β-Bromolaccain	$11_2O_2$ , $CII_3CO_2II$	4-Ketoearboxy-2.3,5-triearboxyphenol (?)	·I	157
10. 2.2.4.4°.Tetranitrobcazil         H202, NaOII         2.4-Dinitrophenol         53           9.10-Phenanthraquinone         H202, NaOII         2.4-Dinitrophenol         53           Benzil         H202, NaOII         Diphenic acid         94           Benzil         CH3C02H         Benzole acid         70           1.3-Diphenylpropane-1,2-dlone         CH3C02H         Benzole acid         70           p-Methoxybenzil         CH3C02H         Benzole acid         83           Anisil         CH4O2H         Anisic acid, blenylacetic acid         61           Anisil         CH4O2H         Anisic acid, blenzole acid         70           Anisil         CH4O2H         Anisic acid, chlyl anisoate         70           Brithhalic acid         Anisic acid, chlyl anisoate         70           Brithhalic acid         Perphthalic acid         2-Styrlacrylic anitydride         66           Brithalic acid         2-Styrlacrylic anitydride         26	$C_{12}H_6U_2$	Acenaphthenequinone	сизсозн	Naplithalle aeld	ı	156
H <sub>2</sub> O <sub>2</sub> , CH <sub>2</sub> CO <sub>2</sub> H   C <sub>1</sub> +Dlultrohenzole acld   Quantitative   H <sub>2</sub> O <sub>2</sub> , NaOH   Diplemic acld   Diplemic	C14H6N4O10	2,2',4,4'.Tetranitrobenzil	II,02, NaOII	2,4-Dinitrophenol	53	57
9.10-Phenanthraquinone   H <sub>2</sub> O <sub>2</sub> , NaOII   Diplication acid   9.4   1     Benzil	;		$\text{II}_2\text{O}_2$ , $\text{CII}_3\text{CO}_2$ II	2,4.Dinitrohenzole acid	Quantitative	ć,
Benzil   B	C14H 902	9,10-Phenanthraquinone	H2O2, NaOII	Dipienie acid	76	136, 156
1.3-Diphenylpropane-1,2-dione CH <sub>2</sub> CO <sub>2</sub> H, HClO <sub>4</sub> Benzolc acid Benzol	C14H10U2	Benzil	C <sub>2</sub> II <sub>5</sub> O <sub>2</sub> H, NaOII	Benzoic acid, ethyl benzoate	0,	158
1.3-Diphenylpropane-1,2-dione C <sub>2</sub> H <sub>2</sub> O <sub>2</sub> H, MoH  p-Methoxybenzil C <sub>2</sub> H <sub>2</sub> O <sub>2</sub> H, NaOH  Anisil Anisi acid, benzole acid  Anisil C <sub>2</sub> H <sub>2</sub> O <sub>2</sub> H, NaOH  Anisi acid, chipi anisoate  H <sub>2</sub> O <sub>2</sub> , CH <sub>2</sub> O <sub>2</sub> H, NaOH  Anisi acid, chipi anisoate  H <sub>2</sub> O <sub>3</sub> , CH <sub>2</sub> O <sub>2</sub> H, NaOH  Anisi acid, chipi anisoate  H <sub>2</sub> O <sub>3</sub> , CH <sub>2</sub> O <sub>3</sub> H, Anisi acid  Perphthalic ac			CH <sub>3</sub> CO <sub>3</sub> H		95	61, 70
1,3-Diphenylptopane-1,2-dione C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> H, NaOH Benzole acld, phenylacetic acld 61 p-Methoxybenzil C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> H, NaOH Anisic acld, benzole acld 79 Anisl C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> H, NaOH Anisic acld, chiyl anisoate 70 H <sub>5</sub> O <sub>2</sub> H, NaOH Anisic acld Anisic acld Bichnamylidenebiacetyi Perphthalic acld 2-Siyrylacrylic aniydride 25 eferences 133-104 are listed on p. 106.	5		H2O2, CH3CO2H, HClO4		83	9
P-recuoxy ventral C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> H, NaOH Aniste celd, benzole acld 79 Anistl C <sub>3</sub> H <sub>3</sub> O <sub>2</sub> H, NaOH Aniste celd, chryl anisonte 70 Dicinnamylidenebiacetyl H <sub>2</sub> O <sub>2</sub> CiI <sub>2</sub> CO <sub>2</sub> H Aniste acld Aniste acld Perphthalic acld 2-Siyrylacrylic aniydride 26 eferences 138-104 are listed on p. 106.	C15 II 202	1,3-1/1pnenylpropane-1,2-dione	C2H5O2H, NaOH	_	61	158
Anist Anista C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> H, NaOH Anista acid, cthyl anisoate 70  H <sub>2</sub> O <sub>2</sub> , OH <sub>2</sub> OO <sub>2</sub> H Anista acid 66  Dicinnamylidenebiacetyi Perphthalic acid 2-Styrylacrylic anitydride 2.6	C H O	p-Medioxy benzii	C2H5O2H, NaOH	٠,	7.9	158
H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> H Anisic acld 66 Dicinnamylidenebjacetyl Perphthalic acld 2-Styrylacrylic anhydride 26 eferences 138-184 are listed on p. 106.	016 H1404	Allish	C2H, O2H, NaOII	•	70	158
Deciminantyndeneoliacetyi Kerphthalle aeld 2-Styrylacrylle anlydride 26 eferences 138-104 are listed on p. 106.	C. H. O.	Diches on off denoting	H2O2, CH3CO2H	Anisic aeld	99	9
	018-1102	Dictalianty indentity and accepts	Perphthalle aeld	2-Styrylacrylle anhydride	56	99
	Note: Ref	erences 138-164 are listed on p. 106.				

TABLE V—Continued

COMPOUNDS
F POLYCARBONYL
OXIDATION C
BAEYER-VILLIGER OXIDATION OF POLYGARBONYL COMPOUNDS

Ŷ	Carbonyl Compound	Reagent	Product	Yicid, %	Kelerence
C <sub>18</sub> H <sub>18</sub> O <sub>2</sub>	1-Mesityl-3-phenylpropane-1,2-dione	c.Diketones—Continued C.H.S.O.H. NAOH CH.CO.2H	ontinued Phenylacetle acld, \$\theta\text{-isoduryle acid} Pelargonle acld, azclale acld Pelargonle acld azlacetle acld acld acid	70 90-95 27	158 61 68
C <sub>19</sub> H <sub>32</sub> O <sub>4</sub> C <sub>21</sub> H <sub>32</sub> O <sub>5</sub>	9,10-Diketostearte en 1,10-Diketostearte grant g	H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> H H <sub>2</sub> O <sub>2</sub> , KHCO <sub>3</sub> H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> H	39,14-Dinydroxy-14-180-17-180etiocholanic acid 39,14-Dinydroxy-14-180-17-180etiocholanic acid 39-Aectoxy-14-18ydroxy-14-18oetiocholanic acid	8 1	68 63
$c_{23}\mathrm{H}_{32}\mathrm{O}_{5}$	36-Acctoxy14-nyuloxy 12 pregnan-21-carboxylle acid lactone	p.Dikelones		1	13
С, П <sub>8</sub> О <sub>2</sub> С, П <sub>10</sub> О <sub>3</sub> С, П <sub>12</sub> О <sub>2</sub>	Acetylacetone Ethyl acetoacctate 3,3-Dimethylpentane-2,4-dlone Ethyl co-methylacetoacetate	CH,CO,H CH,CO,H CH,CO,H CH,CO,H CH,CO,H	Ethyl hydrogen oxalate, ethanol No reaction Ethyl hydrogen oxalate No reaction	11111	11111
HH H H	Ethyl acetonedcarboxylate 2-Acetylindan-1,3-dlone Ethyl benzoylacetate	CH,CO,H H,O, (C,H,),O CH,CO,H	Oxalic actu 2.Acetoxyludun-1,3.dlone 2.Acetoxyludun-1,3.dlone 2.Acetoxyludun-1,3.dlone Ethyl hydogen oxalate, methylbenzyleatblnol	<b>ಪ</b>	20 to to
C <sub>14</sub> H <sub>20</sub> O <sub>2</sub>	Ethyl a-benzylacetoacetate CH <sub>2</sub> —CH <sub>2</sub>	U <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> H	CII,—CII,	55	118
C <sub>15</sub> H <sub>22</sub> O <sub>4</sub> C <sub>16</sub> H <sub>10</sub> O <sub>3</sub> C <sub>17</sub> H <sub>14</sub> O <sub>3</sub> C <sub>27</sub> H <sub>14</sub> O <sub>3</sub>	1-isovalcryl-2,4,6-triketo-3,3,5,5-tetramethyl- H <sub>2</sub> O <sub>2</sub> , pyridlne eyclohexane (leptospermone) 2-Benzoylindan-1,3-dione Acetyldibenzoylmethane H <sub>2</sub> O <sub>2</sub> , (C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C Tribenzoylmethane H <sub>2</sub> O <sub>3</sub> , NaOH	H <sub>2</sub> O <sub>2</sub> , pyridine H <sub>2</sub> O <sub>2</sub> , (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> O H <sub>2</sub> O <sub>2</sub> , (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O H <sub>2</sub> O <sub>2</sub> , NaOH	2,4,0-Triketo-3,3,5,5-tetramethylcyclohoxyl Isovalerate 2-Benzoyloxylndan-1,3-dlone No reaction Benzole acid	51 8 5 5 1 5	70 78 78 78
Note: Re	Z-10. Note: References 138-164 are listed on p. 106.				

TABLE VI
BAEYER-VILLIGER OXIDATION OF ALDEHYDES

the state of the s	Carbonyl Compound	Reagent	Product	Yield, %	Reference
спъ	Formaldehyde	CH <sub>2</sub> CO <sub>3</sub> H	Formic acld	Quantitative	80
0 11 0	Seetaldelivde	6, H, CO, H	Formic acid, hydrogen Acetic acid	1 1	81
		H <sub>2</sub> O <sub>2</sub> , H <sub>2</sub> SO <sub>4</sub>	Acetic acid, formic acid, methane, hydrogen, carbon dioxide	1	88
$C_2\Pi_4O_2$	Glyeolie aldehyde	H <sub>2</sub> O <sub>2</sub>	Hydrogen, carbon dioxide, formic acld, unidentified acids	I	86
$C_2\Pi_gO$	Propionaldehyde	$H_2O_2$ , $H_2SO_4$	Propionic acid, acetic acid, formic acid, hydrogen, carbon dioxide, ethane	1	88
CeIT100	Pivalle aldehyde	<b>Н</b> 202	Isobutane, hydrogen, carbon monoxide, unidentified acids	I	86
C,II,Br,O,	3,5-Dlbromo-2-hydroxybenzaldchyde	H,00, NaOH	3,5-Dibronocatechol	1	52
	3,5-Dibronio-4-liydroxybenzaldehyde	H2O2, NaOH	3,5-Dibromohydroquinone	1	52
	4,6-Dibromo-2-hydroxybenzaldeliyde	11,0, NaOH	4,6-Dibromocatechol	1	52
C,III,CI,O2	3,5-Diehloro-4-hydroxybenzaldehyde	$H_2O_2$ , NaOH	3,5-Dichloroitydroqulnone	1	52
	3,5-Diehloro-2-hydroxybenzaldehyde	H,02, NaOII	3,5-Dichlorocatechol	I	159, 52
$C_7II_4I_2O_2$		H <sub>2</sub> O <sub>2</sub> , NaOH	No reaction	I	22
$C_7II_5BrO_2$		$H_2^{0}0_2$ , NaOII	5-Bromocatechol	I	52
1	3-Bromo-4-hydroxybenzaldehyde	H <sub>2</sub> O <sub>2</sub> , NaOH	Bromohydroguinone	02-09	52
C, 11, C10,	5-Chloro-2-hydroxybenzaldehyde	$H_2O_2$ , NaOH	5-Chlorocatechol	1	52
C, 11, NO.	o-Mitrobenzaldehyde	CH <sub>3</sub> CO <sub>3</sub> H	o-Nitrobenzoie acid	66	91
0% #1 0	m-Nitrobenzaldehyde	сн,со,н	m-Nitrobenzoic acid	06	91
C21151104	3-Miro-2-hydroxybenzaldehyde	H2O2, NaOH	3-Nitrocatechol	1	22
	5-Nitro-2-llydroxybenzaldehyde	H202, NaOH	5-Nitrocatechol	70	52
	S. Vitto Charles and Control of the	H2O2, N2OH	No reaction	: 1	25
	"	H <sub>2</sub> O <sub>2</sub> , NaOH	Nitrobenzoquinone	١	20 1
C.H.O	Non-t-thydroxypenraldehydc	H2O2, NaOH	No reaction	I	7 2
2011	ocuzinanyae	H.SO.	Benzaldchyde peroxide	40	160 140
		H2O2, (C2H5)0	Benzoic acid, phenol	:	99 161
0,11,0	Salleylaldelyde	CH <sub>3</sub> CO <sub>3</sub> H	Benzoic acid	Quantitative	80, 86
Nofe: He	Nofet Unforences 138-164 are listed on m 106	ET 1018111 160811	Sancyne acid, cateenol	70, trace	95
	va p. 100				

## ORGANIC REACTIONS

## TABLE VI-Continued

3 T T T T T T T T T T T T T T T T T T T
OF ALDERITOR
OXIDATION
BAEVER-VILLIGER

	Carbonyl Compound	Reagent	Product	Yleld, %	Reference
	The state of the s				0
0.11.0	Salicylaldehyde (Contd.)	H202, pyridine	Salleylle acid, catechol Catrohol	75, 20 Quantifative	52, I34 102, 91, 95
2001160		CILCO, II	Cateehol	8 1	53
	m-IIydroxybenzaldehyde	H2O2, NaOH	No reaction m-Hydroxybenzoic ackl	74 Quantitative	55 53
	$p ext{-} ext{IIydroxybenzaldelyde}$	11302, NaOH	Ndroqulnone Ndroqulnone	8	80, 91 52
C,11.03	2,4.Dihydroxybenzaldehyde	H2O2, NaOH H2O2, NaOH	Hydroxyhydroquinone Hydroxyhydroquinone Hydroxyhydroquinone	3 1	3 8
C,H,NO C,H <sub>14</sub> 0	o-Amhobenzaldeliyde	11,50, CII,CO,II 11,0, (C,II,),0	o-Aminopheny I tornate, o annuay and na Heptanole acht a-Heptanole acht a-Hydroxyheptylhydroperoxide	I 18	80 11 129
Cg II gO3	Piperonal 2-Hydroxy-4-methylhenzaldehyde	cij.co.ji cii.co.ji	3, t-Methylenedloxyphenol 4-Methyleatechol 5-Methyleatechol	223	E 5 3
C <sub>6</sub> II,BrO <sub>3</sub> C <sub>6</sub> II,NO <sub>5</sub>	2. Hydroxy-6-methymenzharenyae 3. Bromo-4-hydroxy-6-methoxybenzaldehyde 2. Mto-4-hydroxy-3-methoxybenzaldehyde o ving a hwdroxy-6-methoxybenzaldehyde	11,02, Na011 11,02, Na011 11,03, Na011	4-Bromo-5-methoxybydroquinone 3-Methoxy-2-nitrobydroquinone No reaction	? 1 1 1	នេនទ្
C <sub>8</sub> II <sub>8</sub> O	Phenylacetaldehyde	11 <u>.0.</u> 11 <u>.0.</u> beat	Benzyl alcohol, formic acid phenylacette acid, benzaldehyde, formic acid, benzole	11	191
с, 11, 60,	o-Methoxybenzaldehyde	11,0, (C,11,),0 CH,CO,H	aciu Gualacol, o-methoxybenzole acid Gualacol formate	1 66	8 2 8
	$p ext{-}Methoxybenzaldehyde}$	H2O2. (C2H3)20	Hydroquinone monomethyl'ether, p-methoxybenzoic acid	1	1 9
C <sub>6</sub> II <sub>6</sub> O <sub>3</sub>	2-Hydroxy-3-methoxybenzaldehyde 2-Hydroxy-5-nethoxybenzaldehyde 3-Hydroxy-4-methoxybenzaldehyde Vanillin	CII,2CO,1H H <sub>2</sub> O <sub>2</sub> , NaOH H <sub>2</sub> O <sub>2</sub> , NaOH H <sub>2</sub> O <sub>2</sub> , NaOH H <sub>2</sub> O <sub>2</sub> , NaOH	p-Nethoxybenzole neld 3-Nethoxycatechol 4-Nethoxycatechol 4-Nethoxyresocchod (?) Nethoxyhydroqulnone	Quantitutive	158 158 26 26

TABLE VI—Continued

ALDEHYDES
OF
OXIDATION
BAEYER-VILLIGER

	Carbonyl Compound	Reagent	Product	Yleld, %	Reference
C, II 1003	2, t-Dimethoxy benzaldehyde 3,4-Dimethoxy benzaldehyde	$H_2O_2$ , $(C_2H_5)_2O$ $H_2O_2$ , $(C_2H_5)_2O$	2,4-Dimethoxyphenol 3,4-dimethoxybenzoie acid	27	92
C, II, O	Pelargonle aldelyde 3-Ethoxy-4-methoxybenzaldelyde	$H_2O_2$ , $(C_2H_5)_2O$ CH, $CO_3H$	s,t-t/inetitoxypitenoj «-Hydroxynonylhydroperoxide -Ethoxv-t-methoxythenoj	311	90, 91 11 90
C101120 C101120 C101120	2,4,5-Trimethoxybenzaldehyde Caprie aldehyde 3,4-Dimethoxy-G-ethylbenzaldehyde	H <sub>2</sub> O <sub>2</sub> , (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O H <sub>2</sub> O <sub>2</sub> , (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O H <sub>2</sub> O <sub>2</sub> , (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O	2,4,6-Trinethoxyhorory 2,4,6-Trinethoxyhoroproxide 2-Himethoxy-6-ethyhorory 2,1-Hmethoxy-6-	181	92 11 8
Chillao Chillao Chillao	Undecylle aldehyde 4-Butoxy-3-methoxybenzaldehyde	H <sub>2</sub> O <sub>2</sub> , (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O CH <sub>3</sub> CO <sub>3</sub> U	chylbergos occipinator, s.r. uniceloxyo- ethylbergos acid c.Hydroxynndegallydroperoxide 4-Butoxy-3-methoxyphenol	8	92 11 90
C <sub>12</sub> H <sub>21</sub> O C <sub>14</sub> H <sub>11</sub> NO <sub>3</sub> S C <sub>15</sub> H <sub>10</sub> O <sub>2</sub>	Laurle aidelyde 4-Nitro-2(p-tolylthio)benzaldehyde 3-Hydroxy-4-formylphenanthrene	H <sub>2</sub> O <sub>2</sub> , (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O H <sub>2</sub> O <sub>2</sub> , CH <sub>3</sub> CO <sub>2</sub> H H <sub>2</sub> O <sub>2</sub> , NaOH	c-Hydroxydodecylhydroperoxide 4-Nitro-2(p-toluenceulphonyl) benzole aeld 3,4-Dilydroxyphenanthrene	118	11 164 94

Note: References 138-164 are listed on p. 106,

## REFERENCES TO TABLES

- 136 Baoyer and Villiger, Ber., 33, 655 (1900).
- 130 Baever and Villiger, Ber., 33, 124 (1900).
- 100 Dilthey, Inckel, and Stephan, J. pratt. Chem., [2] 154, 219 (1940).
- 111 Friess, J. Am. Chem. Soc., 71, 14 (1949).
- 113 Marker, J. Am. Chem. Soc., 62, 2621 (1940).
- 113 Buchi and Jeger, Helv. Chim. Acta, 32, 540 (1949).
- 111 Karrer and Haab, Helv. Chim. Acta, 32, 973 (1949).
- 115 Schroeter, German pat. 562,827 (Chem. Zente., I. 1933, 127).
- 115 Stoll and Scherrer, Helv. Chim. Acta, 13, 142 (1930).
- 107 Jacobsen, Picha, and Lovy, J. Biol. Chem., 171, 81 (1947).
- 118 Burckhardt and Reichstein, Helv. Chim. Acta, 25, 821 (1942).
- Windaus, Ber., 37, 2027 (1904).
   Dakia, Proc. Chem. Soc., 25, 194 (1909).
- 151 Hassall and Todd, J. Chem. Soc., 1947, 611.
- 152 Inagaki, J. Pharm. Soc. Japan, 59, 7 (1939) [C. A., 33, 3790 (1939)].
- 153 Böeseken and Kremer, Rec. trav. chim., 50, 827 (1931).
- 154 Karrer and Hohl, Hele. Chim. Acta, 32, 1028 (1949).
- 155 Karrer and Testa, Helv. Chim. Acta, 32, 1019 (1949).
- 156 Charrier and Beretta, Gazz. chim. ital., 54, 988 (1924).
- 157 Dimroth and Goldschmidt, Ann., 399, 62 (1913).
- 158 Barnes and Lewis, J. Am. Chem. Soc., 58, 947 (1936).
- 159 Kvalaes, J. Am. Chem. Soc., 56, 2487 (1934).
- 140 Baeyer and Villiger, Ber., 33, 2484 (1900).
- 141 Sandonnini and Giacoraello, Atti reale accad. naz. Lineci, [6] 19, 43 (1934) (Chem. Zentr., II, 1934, 234).
  - 162 Waeek, Eppinger, and Bezard, Ber., 73, 521 (1940).
  - 163 Cattaneo, Gazz. chim. ital., 64, 509 (1934).
  - 164 Campbell, Dick, Ferguson, and Louden, J. Chem. Soc., 1941, 747.

## CHAPTER 4

## THE ALKYLATION OF ESTERS AND NITRILES

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Diethyl Benzylmulonate	\$
Diathyl Ethyl/plany linglangta*	
Diethyl Ethyl(isopropyl)malonate	9
Diethyl Isopropyl(formanido)malonate	í)
Diethyl 1,1-Cyclohutanedicarboxylate	A .
Diethyl 1,1-t velonutalietheartoxylate	a
Diethyl z-Ethyl-z-methylvalerate	1
3-(β-Diethylaroinoethyl)-3-phenyl-2-benrofurnnone	31
Dictivi Ethyl-(1-1-opentenyl)malonate	
Edity (1-Edity property) methy levanoacetate	
istilyi n-putyi(isopropyi)cynnoncetate	
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## INTRODUCTION†

This chapter is concerned with the reactions of metal salts (enclates) of active methylene compounds with alkylating agents such as alkyl halides to produce alkyl derivatives. The first example of this reaction is found in the literature of 1863 when Geuther prepared ethyl  $\alpha$ -ethyl

<sup>\*</sup> To avoid confusion in the aaming of disubstituted netive methylene compounds containing two unlike substituents, the name of one of the substituents has been parenthesized. † The authors are indebted to Morton Brown, Norman A. Le Bel, and Theodor A. Liss for checking the literature referred to in the final draft of this chapter.

This ionic resonance hybrid is often called the enolate anion. It may be formed by reaction of the base with either the keto or the enol form of the active methylene compound.<sup>4</sup>

The acidity of active methylene compounds can be attributed to resonance stabilization of the enolate anion, a stabilizing interaction not possible with the un-ionized form. The degree to which various substituent groups enhance the acidity of active methylene compounds appears to decrease in the following order:  $-NO_2 > -C -R > -C = N > -CO_2C_2H_5 > \frac{1}{N}$ 

-C<sub>6</sub>H<sub>5</sub>. The substitution of two or three such groups on a carbon atom further augments the acidity of the remaining hydrogen atoms bound to the same earbon atom. This effect would be anticipated if the additional resonance stabilization available to such a polysubstituted enolate anion is considered (sec, however, p. 133). On the other hand, substitution of aliphatic groups at the active methylene carbon atom reduces the acidity of the remaining hydrogen atom. The effect of a number of substituents (R) on the acid strength of monosubstituted acetic esters (RCH2CO2C2H5) has been measured;5 the compounds decreased in acidity in the following order:  $R = C_0H_5 > H > CH_3 > C_2H_5 > n \cdot C_3H_7 > n \cdot C_{10}H_{21} > n \cdot C_{16}H_{33}$ > eyelohexyl  $> i \cdot C_3H_7$ . It is noteworthy that branching of the carbon chain  $(R = i \cdot C_3H_7)$  has a greater effect on acidity than the length of the earbon chain (R = n-C<sub>16</sub>H<sub>33</sub>). A similar reduction in the acidity of substituted acetic acids has been ascribed to steric hindrance to solvation of the earboxylate anion.6 This explanation would appear to be equally valid for the increased difficulty with which highly substituted acetic esters are converted to their enolate anions.

The formation of the enolate anion, the reactive derivative of the active methylene compound in alkylation reactions, results from an equilibrium reaction between the base and the active methylene compound. Competing equilibra involve the solvent (i.e., ROH, NH<sub>3</sub>, etc.) and either the base or the enolate anion. As a consequence of these equilibria, both the

$$\begin{array}{c} {\rm B} \, \circ \, + \, {\rm CH_2(CO_2C_2H_5)_2} \rightleftarrows {\rm BH} \, + \, \overset{\odot}{\rm CH(CO_2C_2H_5)_2} \\ \overset{\odot}{\rm CH(CO_2C_2H_5)_2} \, + \, {\rm ROH} \, \rightleftarrows {\rm CH_2(CO_2C_2H_5)_2} \, + \, \overset{\odot}{\rm OR} \\ \\ {\rm B} \, \circ \, + \, {\rm ROH} \, \rightleftarrows {\rm BH} \, + \, \overset{\odot}{\rm OR} \end{array}$$

solvent (i.e., ROH) and the conjugate acid (BH) of the base must be much

<sup>&</sup>lt;sup>4</sup> Alexander, Principles of Ionic Organic Reactions, John Wiley & Sons, New York, 1950, pp. 132-134.

<sup>&</sup>lt;sup>5</sup> Brown and Eberly, J. Am. Chem. Soc., 62, 113 (1940).

<sup>6</sup> Hammond and Hogle, J. Am. Chem. Soc., 77, 338 (1955).

weaker acids than the active methylene compound if an adequate concentration of the enolate anion is to be present in the reaction mixture.

All available evidence indicates that the enolate anion of the active methylene compound reacts with the alkylating agent by a bimolecular nucleophilic displacement  $(S_N 2)$  process.<sup>7-9</sup> Therefore the structure of the alkylating agent may be expected to influence the course of the alkylation reaction in a manner analogous to the effect of structure on other

$$(C_2H_5O_2C)_2CH^{\odot} + \underbrace{ \begin{array}{c} CH_3 \\ C-Br \rightarrow \\ H \end{array}}_{C}$$
 
$$(C_2H_5O_2C)_2CH - C-H + Br^{\odot}$$

 $S_N$ 2 reactions. Thus, inversion of configuration is noted when the displacement occurs at an asymmetric center. Diethyl 3 $\alpha$ -cholestanylmalonate was produced by the reaction of  $3\beta$ -cholestanyl tosylate with

$$p\text{-CH}_3C_6H_4SO_3 \\ H \\ + \text{CH}(CO_2C_2H_5)_2 \\ \longrightarrow \\ (C_2H_5O_2C)_2CH \\ H \\ + \text{CH}(CO_2C_2H_5)_2 \\ \longrightarrow \\ H \\ OH \\ \longrightarrow \\ OH$$

<sup>&</sup>lt;sup>7</sup> Grigsby, Hind, Chanley, and Westheimer, J. Am. Chem. Soc., 64, 2606 (1942).

<sup>&</sup>lt;sup>8</sup> Newman and VanderWerf, J. Am. Chem. Soc., 67, 233 (1945).

Bartlett in Gilman, Organic Chemistry, Vol. 3, John Wiley & Sons, New York, 1953, p. 25.

diethyl sodiomalonate.10 Similarly, the reaction of cyclopentene oxide yielded diethyl trans-(2-hydroxycyclopentyl)malonate.7 The attack of the enolate anion occurs at the less hindered of the two possible positions in ethylene oxides; displacement occurred at the primary earbon atom with both styrene oxide and p-nitrostyrene oxide. 11,12 The hindrance to

$$\begin{array}{c} \text{R} & \overset{\ominus}{\bigcirc} \text{CH-CH}_2 + \overset{\ominus}{\text{CH}} (\text{CO}_2\text{C}_2\text{H}_5)_2 \rightarrow \\ \\ \text{(R = H or NO}_2) & \\ \text{R} & \overset{\ominus}{\bigcirc} \text{CHCH}_2\text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{O} & \text{CO}_2\text{CO}_2\text{CO}_2\text{H}_5 \\ \\ \text{O} & \text{CO}_2\text{CO}_2\text{CO}_2\text{H}_5 \\ \\ \text{O} & \text{CO}_2\text{CO}$$

rearward attack presented by tertiary alkyl halides usually limits the usefulness of the alkylation reaction to primary and secondary alkylating agents (p. 124). When treated with a solution of diethyl sodiomalonate in ethanol, n-butyl bromide, sec-butyl bromide, and t-butyl bromide formed the corresponding diethyl butylmalonates in yields of 80-90%, 13 80-81%, 14 and 6.4%, 15 respectively.

Only in special instances has the course of the reaction deviated from the path expected on the basis of a normal bimolecular nucleophilic displacement. The reaction of certain allyl halides with enolate anions has been observed to yield mixtures of products. Although 1-chloro-2-pentene reacted with the diethyl malonate anion to yield only the expected product, the isomeric 3-chloro-1-pentene formed both the product of direct displacement and the product resulting from attack of the enolate at the 1-position in an SN2' displacement. 16,17

<sup>16</sup> Shoppes and Stephenson, J. Chem. Soc., 1954, 2231.

<sup>11</sup> Van Zyl and van Tamelen, J. Am. Chem. Soc., 72, 1357 (1950).

<sup>11</sup> Cristol and Helmreich, J. Am. Chem. Soc., 74, 4083 (1952).

<sup>11</sup> Adams and Kamm, Org. Syntheses, Coll. Vol. 1, John Wiley & Sons, New York, 1941,

<sup>14</sup> Vict, Marvel, and Hauch, Org. Syntheses, Coll. Vol. 2, John Wiley & Sons, New York, 1943, p. 417.

<sup>&</sup>lt;sup>14</sup> D.x and Bywater, J. Am. Chem. Soc., 58, 731 (1936).

<sup>14</sup> Winstein, Bull. soc. chim. France, 1951, C43.

<sup>&</sup>lt;sup>17</sup> Kepner, Winstein, and Young, J. Am. Chem. Soc., 71, 115 (1949).

When, in similar systems, the halogen was bonded to a tertiary carbon atom, as in linally chloride<sup>18</sup> or linally bromide,<sup>19</sup> only the product resulting from an  $S_N 2'$  displacement was observed.

$$(\mathrm{CH_3})_2\mathrm{C} = \mathrm{CHCH_2CH_2CH_2CH_2CH_2CH_2} + \overset{\ominus}{\mathrm{CH}}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2 \rightarrow$$
 
$$(\mathrm{CH_3})_2\mathrm{C} = \mathrm{CHCH_2CH_2CH_2C(CH_3)} = \mathrm{CHCH_2CH(CO}_2\mathrm{C}_2\mathrm{H}_5)_2$$

$$(C_2H_5O_2C)_2CH$$

$$CH_3$$

$$CH_4$$

$$CH_3$$

$$CH_3$$

$$CH_4$$

$$CH$$

<sup>18</sup> Barnard and Bateman, J. Chem. Soc., 1950, 926.

<sup>19</sup> Dupont and Labaune, Chem. Zentr., 82, II, 138 (1911).

A displacement of the  $S_N2'$  type has been postulated to explain the products formed when 1,4-dibromo-2-butene reacted with diethyl sodiomalonate (p. 141).20 A more complicated example of an abnormal alkylation is provided by the reaction of  $3\beta$ -cholesteryl tosylate with diethyl sodiomalonate. The products initially reported, 21,22 diethyl 3-cholesterylmalonate (later shown to be the \alpha-isomer^{10}) and diethyl 3,5-cyclo-6-cholestanylmalonate, seemed best explained by the simultaneous operation of  $S_N^2$  and  $S_N^2'$  displacements.<sup>23</sup> However, the demonstration<sup>10</sup> that the diethyl 3-cholesterylmalonate fraction is composed mainly of the 3  $\beta$ -isomer suggests the intervention of an intermediate cholesteryl ion (shown in brackets in the equation on page 113) prior to attack by the enolate anion. A similar anomaly was observed when  $\beta$ -haloamines were used as alkylating agents. When diphenylacetonitrile was alkylated either with 1-dimethylamino-2-chloropropane or with 2dimethylamino-1-chloropropane similar mixtures of products were obtained.24-26 Such a result suggests the formation of a cyclic immonium ion<sup>27</sup> prior to the alkylation step.

 $(C_6H_5)_2C(CN)CH(CH_3)CH_2N(CH_3)_2 + (C_6H_5)_2C(CN)CH_2CH(CH_3)N(CH_3)_2$ 

The alkylation of alkylidene derivatives may be considered a variant of the reaction of monoalkylated sodiomalonic esters with alkylating agents. With the alkylidene derivatives the alkyl group is invariably introduced at the position alpha to the activating group with attendant migration of the double bond to the  $\beta,\gamma$ -position.<sup>28</sup>

<sup>&</sup>lt;sup>20</sup> Kierstead, Linstead, and Weedon, J. Chem. Soc., 1952, 3610.

<sup>&</sup>lt;sup>21</sup> Kaiser and Svarz, J. Am. Chem. Soc., 67, 1309 (1945).

<sup>22</sup> Swarz and Kaiser, J. Am. Chem. Soc., 69, 847 (1947).

<sup>22</sup> Corey and Sneen, J. Am. Chem. Soc., 75, 6234 (1953). 24 Schultz and Sprague, J. Am. Chem. Soc., 70, 48 (1948).

<sup>23</sup> Attenburrow, Elks, Hems, and Speyer, J. Chem. Soc., 1949, 510.

<sup>24</sup> Walton, Ofner, and Thorp, J. Chem. Soc., 1949, 648. 27 Schultz, Robb, and Sprague, J. Am. Chem. Soc., 69, 2454 (1947).

<sup>18</sup> Cope, Hartung, Hancock, and Crossley, J. Am. Chem. Soc., 62, 314 (1940).

$$\begin{array}{c} \mathrm{CH_{3}CH_{2}CH} \!\!=\!\! \mathrm{C}(\mathrm{CO}_{2}\mathrm{C}_{2}\mathrm{H}_{5})_{2} + \overset{\circ}{\mathrm{O}}\mathrm{C}_{2}\mathrm{H}_{5} \rightleftarrows \mathrm{C}_{2}\mathrm{H}_{5}\mathrm{OH} + \\ & \overset{\circ}{\mathrm{COC}_{2}\mathrm{H}_{5}} \\ \mathrm{CH_{3}CHCH} \!\!=\!\! \mathrm{C} \\ & \overset{\circ}{\mathrm{COC}_{2}\mathrm{H}_{5}} \\ & \overset{\circ}{\mathrm{COC}_{2}\mathrm{H}_{5}} \\ & \overset{\circ}{\mathrm{O}} \\ & \overset{\circ}{\mathrm{O}} \\ & \overset{\circ}{\mathrm{COC}_{2}\mathrm{H}_{5}} \\ & \overset{\circ}{\mathrm{O}} \\ & \overset{\circ}{\mathrm{O}}$$

## SCOPE AND LIMITATIONS

## General Considerations

Nature of the Base and Solvent. If an alkylation reaction proceeds by the bimolecular mechanism described earlier (p. 111), the rate of alkylation will be directly proportional to the molar concentration of the enolate ion present in the reaction mixture. When the enolate concentration is small, various side reactions, to be described later (p. 123), will predominate. Since the concentration of the enolate ion is dependent upon equilibria involving the base, the solvent, and the active methylene compound (p. 110), the correct choice of base and solvent is of prime importance if the alkylation reaction is to be successful. Usually the base and solvent chosen are such that both the conjugate acid of the base and the solvent are weaker acids than the active methylene compound. Such a choice assures a high concentration of the enolate anion.

In several instances the rate of alkylation of  $\beta$ -keto esters has been found to depend on the nature of the cationic portion of the base employed.<sup>29</sup> This effect has been ascribed to the formation of a chelate structure, composed of the cation and the coolate anion, which subsequently reacts

with the alkyl halide.29 Alternatively, the effect of the cation on the rate of alkylation might be attributed to the association of the cation and the enolate anion as ion pairs in the non-polar solvents where the effect of the cation is most pronounced.30 If such ion pairs are less effective than the free enolate anions as nucleophilic reagents, then the rate of alkylation would depend on the extent to which the cation and enolate anion are associated as ion pairs, a property which would be a function of the particular cation employed in a given solvent system.

The reagents most commonly used to prepare the enolates of active methylene compounds include the metal alkoxides and the more basic metal amides, sodium triphenylmethide and sodium hydride, as well as metallic sodium and metallic potassium. A meaningful comparison of relative base strengths can best be made in terms of various base-solvent systems, since the basicity is influenced by the solvent. Many of the comparisons of relative basicity made in this chapter are founded on the success or failure of various bases in certain alkylation reactions, because data concerning relative basicities are not available. Consideration of the enolate-base-solvent equilibria mentioned earlier (p. 110) will make apparent the possibility of increasing the concentration of the enolate anion in the reaction mixture if the solvent is replaced by a solvent of lower acidity. This possibility has been exploited in several instances 31-33 where alkylation was either unsuccessful or difficult with alcohol as the solvent; replacement of the alcohol with a less acidic solvent such as ether or benzene permitted alkylation to occur. If possible, the base and the enolate should be soluble in the solvent chosen. Otherwise, the surface of the basic reagent may become coated with the metal enolate, preventing further reaction.

The metal alkoxides are usually sufficiently strong bases for use in the alkylation of malonic esters, cyanoacetic esters, malononitriles, and certain mononitriles. The commonly employed metal alkoxides appear to increase in basicity in the following order:34-37 CH<sub>3</sub>ONa < CH<sub>3</sub>CH<sub>2</sub>ONa < (CH<sub>3</sub>)<sub>2</sub>CHONa < (CH<sub>3</sub>)<sub>3</sub>COK. When the active methylene compound and/or the alkylating agent contain one or more ester functions, the alkoxide chosen should correspond to the alkoxyl group of the ester.

<sup>29</sup> Bründstrom, Acta Chem. Scand., 7, 223 (1953).

<sup>&</sup>lt;sup>20</sup> James Cason, private communication.

<sup>&</sup>lt;sup>21</sup> Wagner-Jauregg and Arnold, Ann., 529, 274 (1937).

<sup>&</sup>lt;sup>12</sup> Adams, Stanley, and Stearns. J. Am. Chem. Soc., 50, 1475 (1928). <sup>21</sup> Pearson, J. Am. Chem. Soc., 71, 2212 (1949).

<sup>34</sup> Janeson, Ann., 250, 125 (1888).

<sup>35</sup> Kopp and Tchoubar, Bull. soc. chim. France, 1951, 30. 36 McEwen, J. Am. Chem. Soc., 58, 1124 (1936).

<sup>&</sup>lt;sup>27</sup> Cope and Hancock, J. Am. Chem. Soc., 60, 2903 (1938).

Otherwise a nonhomogeneous product will result from the ester interchange which takes place concurrently with alkylation.<sup>37–41</sup> This problem

$$\begin{array}{c} \mathrm{CH_2(CN)CO_2C_2H_5} + i \cdot \mathrm{C_5H_{11}O} & \Rightarrow \mathrm{CH_2(CN)CO_2C_2H_5} \\ & & \downarrow \\ & & \mathrm{CC_5H_{11}} \cdot i \end{array}$$
 
$$\mathrm{C_2H_5O} & + \mathrm{CH_2(CN)CO_2C_5H_{11}} \cdot i \end{array}$$

is least serious when the highly branched t-butoxide anion is employed. Several cases have been reported in which the use of sodium t-butoxide in t-butyl alcohol led to the successful alkylation of ethyl esters that could not be alkylated readily with sodium ethoxide in ethanol.<sup>35</sup>

The sodium and potassium alkoxides are normally prepared and used in an excess of the corresponding anhydrous  $^{13,42}$  alcohol which serves as the solvent. However, the advantages to be gained from the use of other solvents should not be overlooked. The decarbethoxylation of malonic and cyanoacetic esters in the presence of ethoxide ion, to be discussed more fully later (p. 127), which sometimes occurs as a side reaction, can be diminished if diethyl carbonate is used as the reaction solvent.  $^{43,44}$  In addition, the high boiling point of diethyl carbonate permits the reaction time to be shortened. In general, the low yields obtained from slow alkylation reactions (e.g., with long-chain alkyl halides as the alkylating agents) are improved if the low-boiling solvent, ethanol or ether, is replaced by a higher-boiling solvent such as n-butyl alcohol  $^{45,46}$  or diethyl carbonate,  $^{43,44,47-51}$  or if the reaction mixture is heated in a sealed tube.  $^{31,52}$  However, higher reaction temperatures sometimes favor dialkylation  $^{53}$  and dehydrohalogenation of the alkylating agent.  $^{54}$ 

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Hessler, J. Am. Chem. Soc., 38, 909 (1916).
Hessler and Lamb, J. Am. Chem. Soc., 43, 205 (1921).
Hessler and Henderson, J. Am. Chem. Soc., 43, 672 (1921).
Osman and Cope, J. Am. Chem. Soc., 66, 881 (1944).
Gyngell, Phillips, and Smith, Ind. Chemist, 21, 526 (1945).
Wallingford, Homeyer, and Jones, J. Am. Chem. Soc., 63, 2056 (1941).
Wallingford, Thorpe, and Homeyer, J. Am. Chem. Soc., 64, 580 (1942).
Bleyberg and Ulrich, Ber., 64, 2504 (1931).
Backer and Strating, Rec. trav. chim., 59, 933 (1940).
Simon, Kaufmann, and Schinz, Helv. Chim. Acta, 29, 1133 (1946).
Plattner, Fürst, Wyss, and Sandrin, Helv. Chim. Acta, 30, 689 (1947).
Wiss and Fuchs, Helv. Chim. Acta, 35, 407 (1952).
Blicke and Leonard, J. Am. Chem. Soc., 68, 1934 (1946).
Wallingford and Homeyer, U.S. pat. 2,358,768 [C. A., 39, 1879 (1945)].
Marshall, J. Chem. Soc., 1931, 2336.
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53 Ziegler and Ohlinger, Ann., 495, 84 (1932).

54 Cope and McElvain, J. Am. Chem. Soc., 54, 4311 (1932).

The increase in the enolate concentration which results when an alcohol is replaced by a much less acidic or an inert solvent has already been mentioned (p. 116). However, the sodium and potassium alkoxides are relatively insoluble in such inert solvents. Magnesium ethoxide, being soluble in inert solvents, 55,56 offers an advantage in this respect. This base, which readily converts diethyl malonate to its enolate, 57 is of especial value for the dialkylation of this ester. 55,56

The use of sodium hydride in benzene, toluene, or dimethylformamide is particularly advantageous in alkylation reactions. Sodium hydride reacts irreversibly with an active methylene compound to form an enolate and hydrogen; it has been shown that any sodium hydride which may remain has no effect upon a wide variety of alkyl halides even after prolonged times at elevated temperatures. 58

Sodium amide is generally used to prepare the sodium derivatives of mononitriles, 53,59 some monocarboxylic esters, 60-62 some alkylmalonic esters, and alkylidenemalonic esters derived from ketones. 63,64 The lithium, sodium, and bromomagnesium salts of secondary amines have found limited use as bases in the alkylation of mononitriles. 53,65,66 The use of lithium diethylamide rather than sodium amide as the base for the alkylation of nitriles avoids side reactions involving addition of the amide ion to the nitrile group (p. 129).53 This side reaction is particularly serious with disubstituted acetonitriles.

The alkylation of monocarboxylic esters is usually effected in the presence of the strong base sodium triphenylmethide. 67-70 Reactions which employ either sodium amide or sodium triphenylmethide as the base require an inert solvent such as ether, benzene, toluene, or

Metallic sodium and metallic potassium in inert solvents have been used

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ss Lund, Ber., 67, 935 (1934).
  56 Lund, Hansen, and Voigt, Kgl. Danske Videnskab. Selskab, Mat-fys. Medd., 12, No. 9,
23 (1933) [C. A., 28, 2333 (1934)].
  <sup>57</sup> Walker and Hauser, J. Am. Chem. Soc., 68, 1386 (1946).
  58 Cristol, Ragsdale, and Meek, J. Am. Chem. Soc., 71, 1863 (1949).
   59 Ramart, Compt. Rend., 182, 1226 (1926).
  60 Ramart and Amagat, Ann. chim. Paris, [10] 8, 273 (1927).
  41 Ramart, Bull. soc., chim. France, [4] 35, 196 (1924).
   62 Ramart, Compt. rend., 178, 396 (1924).
   43 Cope and Hancock, J. Am. Chem. Soc., 60, 2644 (1938).
   64 Cope, Hofmann, and Hardy, J. Am. Chem. Soc., 63, 1852 (1941).
   45 Cason, Sumrell, and Mitchell, J. Org. Chem., 15, 850 (1950).
   56 Ziegler, Fr. pat. 581,728 [C. A., 27, 4251 (1933)].
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<sup>&</sup>lt;sup>57</sup> Schlenk, Hillemann, and Rodloff, Ann., 487, 135 (1931). 44 Hudson and Hauser, J. Am. Chem. Soc., 62, 2457 (1940).

<sup>49</sup> Hudson and Hauser, J. Am. Chem. Soc., 63, 3156 (1941). 70 Polgar and Robinson, J. Chem. Soc., 1943, 615.

Exertensively to prepare the enolates of malonic ester, cyanoacetic ester, and 3-aryl-2-benzofuranones. Several attempts to use metallic sodium in the alkylation of aliphatic mononitriles have resulted in dimerization of the nitrile. The alkylation of aliphatic mononitriles have resulted in dimerization of the special potassium must be avoided as bases for the alkylation of alkylidenemalonic and alkylidenecyanoacetic esters because partial reduction of the conjugated system accompanies enolate formation. 28,37,63,74

Sodium hydroxide and potassium hydroxide have been employed as bases for the alkylation of active methylene compounds. The alkylation of nitriles, in certain instances at least, appears to offer no complications with these bases. 34,75-79 Although extensive saponification would be expected to attend the alkylation of esters in the presence of potassium hydroxide, successful alkylations with this base have been reported by several workers. 80-83 These alkylations were usually effected by treatment of the active methylene compound with a suspension of powdered potassium hydroxide in an inert solvent such as di-n-propyl acetal followed by addition of an alkyl halide. For example, ethyl cyanoacetate was converted to ethyl benzylcyanoacetate in 30% yield by this procedure. 83

Other bases that have had limited use include benzyltriethylammonium hydroxide, <sup>84</sup> potassium acetate, <sup>85</sup> ammonia, <sup>86,87</sup> potassium carbonate, <sup>88,89</sup> phenylsodium, <sup>90</sup> and various sodium enolates. <sup>91–93</sup> Alkylations have also been effected in the presence of metallic zinc <sup>94</sup> and inorganic salts of

71 Hanriot and Bouveault, Bull. soc. chim. France, [3] 1, 170 (1889).

72 Wache, Jahresber., 1889, 644.

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73 Holtzwart, J. prakt. Chem. [2] 39, 230 (1889).
74 Hugh and Kon, J. Chem. Soc., 1930, 775.
75 von Braun, Fussgänger, and Kühn, Ann., 445, 201 (1925).
<sup>76</sup> Zelinsky and Feldmann, Ber., 22, 3290 (1889).
<sup>77</sup> Eisleb, Ber., 74, 1433 (1941).
<sup>78</sup> Cloke, J. Am. Chem. Soc., 51, 1174 (1929).
79 Pickard and Yates, J. Chem. Soc., 95, 1011 (1909).
80 Ingold, J. Chem. Soc., 119, 305 (1921).
81 Woizmann, Bergmann, and Sulzbacher, J. Org. Chem., 15, 918 (1950).
82 Miehael, J. prakt. Chem., [2] 72, 537 (1905).
83 Weizmann, Brit. pat. 582,191 [C. A., 41, 2436 (1947)].
84 Jarrousse, Compt. rend., 232, 1424 (1951).
85 Kohler, Hill, and Bigelow, J. Am. Chem. Soc., 39, 2405 (1917).
86 Kohler and Conant, J. Am. Chem. Soc., 39, 1404 (1917).
87 Kötz, J. prakt. Chem., [2] 75, 433 (1907).
88 Pettersson, Acta Chem. Scand., 4, 1319 (1950) [C. A., 47, 3847 (1953)].
89 Robinson, J. Chem. Soc., 125, 226 (1924).
<sup>90</sup> Bockmühl and Ehrhardt, Ger. pat. 622,875 [C. A., 30, 2991 (1936)].
<sup>91</sup> Bockmühl and Ehrhaert, Ann., 561, 52 (1948).
92 Case, J. Am. Chem. Soc., 55, 2927 (1933).
93 Boekmühl and Ehrhardt, U.S. pat., 2,230,774 [C. A., 35, 3391 (1941)].
94 Shukowski, J. Russ. Phys. Chem. Soc., 1887 (1), 601; Ber., 21, Ref. 57 (1888).
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silver. 95,96 The yields in several alkylation reactions have been improved when copper or a copper salt was added to the reaction mixture. 97-100

Monoalkylation versus Dialkylation. During the alkylation of diethyl sodiomalonate with ethyl bromide, the diethyl ethylmalonate that is

(1) 
$$CH_2(CO_2C_2H_5)_2 + C_2H_5O = CH(CO_2C_2H_5)_2 + C_2H_5OH$$

(2) 
$$\overset{\odot}{\text{CH}}(\text{CO}_2\text{C}_2\text{H}_5)_2 + \text{C}_2\text{H}_5\text{Br} \rightarrow \text{C}_2\text{H}_5\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 + \text{Br}^{\odot}$$

$${}^{(4)} \ C_2H_5\overset{\circ}{C}(CO_2C_2H_5)_2 + C_2H_5OH \rightleftarrows C_2H_5CH(CO_2C_2H_5)_2 + C_2H_5O^{\circ}$$

$${\rm (5)} \ \ {\rm C_2H_5C(CO_2C_2H_5)_2} + \ {\rm C_2H_5Br} \rightarrow {\rm (C_2H_5)_2C(CO_2C_2H_5)_2} + \ {\rm Br}^{\odot}$$

formed (reaction 2) is in equilibrium with its anion (reactions 3 and 4). The question, therefore, arises as to why little dialkylation (reaction 5) is observed. In a competitive experiment diethyl malonate was alkylated by ethyl bromide (reaction 2) at a rate seventy times the rate of alkylation of diethyl ethylmalonate (reaction 5).<sup>33</sup> The ratio of the ionization constants<sup>33</sup> of the two esters

$$\frac{K_{\rm dicthyl \; malonate}}{K_{\rm dicthyl \; ethyl malonate}} = \frac{1.6 \times 10^{-18}}{2 \times 10^{-20}} \sim 10^2$$

indicates that the concentration of diethyl malonate enolate exceeds the concentration of the diethyl ethylmalonate anion.

Of much greater importance here is the acidity of the solvent, ethanol (K ionization =  $7.28 \times 10^{-20}$ ). Ior As ean be seen from the enolate-base-solvent equilibria mentioned earlier (p. 110), a solvent that is more acidic than the active methylene compound will greatly reduce the

concentration of enolate present in the reaction mixture since the molar concentration of the solvent is much larger than the molar concentration of the active methylene compound. In the alkylation of diethyl malonate with ethyl bromide, the presence of a large excess of ethanol in the reaction mixture reduces the concentration of the enolate of diethyl ethylmalonate to such a low level that the rate of dialkylation (reaction 5) becomes negligible. As would be predicted on this basis, the replacement of ethanol with an inert solvent favors dialkylation.  $^{102}$  As would be expected from the facts mentioned above, the greater acidities of alkylcyanoacetic esters and alkylmalonitriles (for malononitrile K ionization  $\sim 10^{-11}$ )  $^{103}$  cause dialkylation to be a more serious problem.  $^{95}$ ,  $^{104}$ – $^{106}$ 

Dialkylation also becomes an important side reaction in the alkylation of active methylene compounds with very reactive halogen compounds such as benzyl halides,  $^{95,107-119}$  allyl halides,  $^{53,56,120-122}$  phenacyl halides,  $^{56,106,123,124}$  and  $\alpha$ -chloro thio ethers. The large amount of dialkylation observed with the allyl or benzyl halides or with  $\alpha$ -halo ethers may be attributed to the fact that heterolytic cleavage of the carbonhalogen bond in such compounds during bimolecular displacement reactions may occur without substantial aid from the attacking nucleophilic reagent. Therefore, a halide of this type (e.g., benzyl chloride) would be expected to show less discrimination between two nucleophilic

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102 Clemo and Tenniswood, J. Chem. Soc., 1931, 2549.
  103 Branch and Calvin, The Theory of Organic Chemistry, Prentice-Hall, New York.
1941, p. 269.
  104 Hesse, Am. Chem. J., 18, 723 (1896).
  105 Cohen, Marshall, and Woodman, J. Chem. Soc., 107, 887 (1915).
  105 Rây and Ray, J. Chem. Soc., 127, 2721 (1925).
  107 Bisehoff and Siebert, Ann., 239, 92 (1887).
  108 Fittig and Röders, Ann., 256, 87 (1890).
  109 Hausmann, Ber., 22, 2019 (1889).
  110 Poppe, Ber., 23, 108 (1890).
  111 Cassirer, Ber., 25, 3018 (1892).
  112 Reissert, Ber., 29, 633 (1896).
  113 Maxim, Bull. soc. chim. France, [4] 39, 1024 (1926).
  114 Fieser and Seligman, J. Am. Chem. Soc., 57, 942 (1935).
  115 Kenner and Witham, J. Chem. Soc., 119, 1452 (1921).
  116 Walker, J. Chem. Soc., 125, 1622 (1924).
  117 Gulland, Haworth, Virden, and Callow, J. Chem. Soc., 1929, 1666.
  118 Curtius and Mülhäusser, J. prakt. Chem., [2] 125, 291 (1930).
  119 Marvel, Org. Syntheses, 21, 99 (1941).
  120 Paul and Cottin, Bull. soc. chim. France, [5] 4, 933 (1937).

    Paul and Cottin, Bull. soc. chim. France, 19, 2, 44
    Paul and Cottin, Bull. soc. chim. France, 19, 2, 44
    McBay, Jenkins, and Data, J. Am. Pharm. Assoc., 39, 138 (1950) [C. A., 44, 4870]

(1950)].
  122 Ziegler, Fr. pat. 728,241 [C. A., 26, 5573 (1932)].
  123 Klobb, Ann. chim. Paris, [7] 10, 168 (1897).
```

124 Thorpe, J. Chem. Soc., 91, 1004 (1907).

Walter, Goodson, and Fosbinder, J. Am. Chem. Soc., 67, 655 (1945).
 Walter, Goodson, and Fosbinder, J. Am. Chem. Soc., 67, 657 (1945).

reagents (e.g., the sodium enolate of diethyl malonate and the more hindered sodium enolate of diethyl benzylmalonate) than would a saturated alkyl halide (e.g., n-butyl chloride; cleavage of the carbon-chlorine bond in this case would be greatly facilitated by the attacking nucleophilic reagent).

In addition to the foregoing suggestion, a second factor may account for the large amount of dialkylation observed with phenacyl halides. A monoalkylated product such as diethyl phenacylmalonate would be expected to be more acidic than a monoalkyl derivative such as diethyl ethylmalonate because of the proximity of an electron-withdrawing carbonyl function in the former example. For this reason the proportion of diethyl phenacylmalonate converted to its sodium enolate, a necessary intermediate for dialkylation, would be larger than the proportion of diethyl ethylmalonate converted to its sodium enolate under comparable conditions.

As the reaction leading to the alkylation of an active methylene compound (Z-CH<sub>2</sub>-Y) proceeds, the ratio of the concentration of the monosubstituted enolate [R—C(Z)Y] to the concentration of the unsubstituted enolate (Z—CH—Y) must necessarily increase. An increase in this ratio will increase the proportion of dialkylation that occurs. This unfavorable

$$Z \stackrel{\circ}{-CH} - Y + R - CH(Z)Y \rightleftharpoons Z - CH_2 - Y + R - C(Z)Y$$

$$\frac{[R - C(Z)Y]}{[Z - CH - Y]} = \frac{K[R - CH(Z)Y]}{[Z - CH_2 - Y]}$$

concentration ratio may be overcome to a large extent if an excess of the active methylene compound (Z—CH<sub>2</sub>—Y) is used,7,33,105,116,118,127-135 a possibility first realized by Leuchs. 136 Dialkylation has also been diminished by the addition of an excess of both the active methylene

<sup>127</sup> Gagnon, Boivin, and Boivin, Can. J. Research, 28B, 207 (1950).

<sup>111</sup> Gagnon, Boivin, and Giguère, Can. J. Research, 28B, 352 (1950). 129 Skinner, J. Am. Chem. Soc., 59, 322 (1937).

<sup>110</sup> Huber, Clinton, Bochme, and Jackman, J. Am. Chem. Soc., 67, 1018 (1945). 111 Gol'mov, Zhur. Obshchel Khim. (J. Gen. Chem. U.S.S.R.), 19, 1679 (1949) [C. A., 44] 1030 (1950)].

<sup>111</sup> Olynyk, Camp, Griffith, Woislowski, and Helmkamp, J. Org. Chem., 13, 465 (1948). 121 Curtius and Gaier, J. prakt. Chem., [2] 125, 279 (1930).

<sup>134</sup> Brigl, Hopps Scyler's Z. physiol. Chem., 95, 161 (1915).

<sup>131</sup> Weitzel and Wojalin, Hopps-Seyler's Z. physiol. Chem., 285, 220 (1950).

compound and the base; such additions serve to increase the concentration of the active methylene enolate (Z—CH—Y). $^{112,124,137-139}$ 

Other factors reported to favor monoal kylation include the use of low-boiling solvents  $^{53}$  and the use of alkyl chlorides rather than alkyl bromides.  $^{140}$ 

Order of Introduction of Groups. If two alkyl groups are to be introduced into malonic or cyanoacetic ester, the order of introduction of groups may have a profound influence on the yield and purity of the product. When the two alkyl groups are identical best results have been obtained by adding one equivalent of the base and alkyl halide, allowing the reaction mixture to become approximately neutral, and then adding the second equivalent of base and alkyl halide. Where two different alkyl residues are to be introduced, it is advisable to introduce the larger group first if both alkylation steps involve displacement at a primary carbon atom. This order is of particular importance if the smaller alkyl residue is a methyl or an ethyl group; in these cases the boiling points of the unchanged ester, the monoalkylated ester, and the dialkylated ester are too close to one another to permit separation without recourse either to very precise fractional distillation of the control of the entire to the course of the course either to very precise fractional distillation.

In the dialkylation of malonic ester the introduction of a primary alkyl group should always precede the introduction of a secondary alkyl group. If this precaution is not observed the introduction of a second alkyl group is often unsuccessful,<sup>35,145-149</sup> because of the low acidity of the intermediate sec-alkylmalonic ester (p. 110) and the sterically hindered nature of the corresponding enolate anion. This difficulty accompanying the alkylation of sec-alkylmalonic esters has occasionally been overcome by the use of a strong base such as sodium t-butoxide in t-butyl alcohol.<sup>35</sup>

Side Reactions. Aside from dialkylation, a wide variety of side reactions may attend the alkylation of an active methylene compound. Among these side reactions are the reactions of the alkylating agent with the base

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137 Hinegardner and Johnson, J. Am. Chem. Soc., 52, 3724 (1930).
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<sup>138</sup> Leveno and Allen, J. Biol. Chem., 27, 433 (1916).

<sup>139</sup> Zaheer and Sidhu, J. Indian Chem. Soc., 24, 134 (1947).

<sup>140</sup> Hinegardner and Johnson, J. Am. Chem. Soc., 52, 4139 (1930).

<sup>141</sup> Leveno and Cretcher, J. Biol. Chem., 33, 505 (1918).

<sup>142</sup> Dolique, Ann. chim. Paris, [10], 15, 429 (1931).

<sup>143</sup> Dolique, Compt. rend., 190, 878 (1930).

<sup>144</sup> Dox and Yoder, J. Am. Chem. Soc., 44, 1141 (1922).

<sup>145</sup> Crossley and Le Sueur, J. Chem. Soc., 77, 83 (1900).

<sup>&</sup>lt;sup>146</sup> Kondakova and Katsnel'son, Compt. rend. acad. sci. (U.R.S.S.) N.S., 4, 403 (1936)
[C. A., 31, 3448 (1937)].

<sup>&</sup>lt;sup>147</sup> Zelinskii, Bondar, Kost, and Lifshits, Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, (1951), No. 2, 96 [C. A., 45, 10205 (1951)].

<sup>&</sup>lt;sup>148</sup> Shonle, Keltch, and Swanson, J. Am. Chem. Soc., 52, 2440 (1930).

<sup>149</sup> Hope and Perkin, J. Chem. Soc., 95, 1360 (1909).

and solvent. Provided that an adequate concentration of the enolate anion is present (p. 115) the interaction of the alkylating agent and the solvent and/or the base to produce an ether becomes a serious competing reaction only with very reactive halides such as allyl, 150-152 benzyl, 153,154 and benzhydryl halides. The low yields obtained in the synthesis of benzhydrylmalonic esters, presumably attributable to solvolysis of the benzhydryl halides in the alcoholic reaction mixture, 155 may be avoided if the reaction is conducted in benzene solution. 156 Triphenylmethyl chloride also has served as an effective alkylating agent in ether solution.56

As was noted earlier (p. 112) tertiary alkyl halides that can undergo dehydrohalogenation usually do so more rapidly than they undergo the displacement reaction leading to alkylation; accordingly, they are poor alkylating agents. 157,159 Olefin formation is less important with secondary alkyl halides and is not a serious side reaction with primary alkyl halides. Halogen compounds like ethyl α-bromoisobutyrate<sup>161</sup>—167 and ethyl  $\beta$ -bromolevulinate<sup>168</sup> whose dehydrohalogenation leads to an  $\alpha,\beta$ -unsaturated ester or ketone introduce a further complication; the initially formed unsaturated products may add the active methylene compound in a Michael reaction. 161,162

 $\overset{\odot}{\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2}} \\ + (\text{CH}_3)_2\text{CBrCO}_2\text{C}_2\text{H}_5 \\ & \xrightarrow{\text{Dehydrohalogenation}} \\ & \xrightarrow{\text{CH}_2 = \text{C}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5}}$ CH2(CO2C2H2)2  $\cdot \mathrm{(C_2H_5O_2C)_2CHCH_2CH(CH_3)CO_2C_2H_5}$ 

150 Mousseron and Winternitz, Bull. soc. chim. France, 1946, 604.

151 Perkins and Cruz, J. Am. Chem. Soc., 49, 517 (1927).

152 Kierstead, Linstead, and Weedon, J. Chem. Soc., 1953, 1803. 153 Mayer, Sieglitz, Fischer, Hagen, Jung, Knies, Kohl, Listmann, Neugebauer, and Schulte, Ber., 55, 1835 (1922).

154 de Benneville, Clagett, and Connor, J. Org. Chem., 6, 690 (1941).

155 Hammett, Physical Organic Chemistry, McGraw-Hill Book Co., New York, 1940, p. 167. 136 Cope, J. Am. Chem. Soc., 56, 721 (1934).

157 Widegvist, Arkiv Kemi, Mineral. Geol., B23, No. 4, 6 (1946) [C. A., 41, 1615 (1947)]. 158 St. Pfau and Plattner, Helv. Chim. Acta, 22, 202 (1939).

139 Alexander, McCollum, and Paul, J. Am. Chem. Soc., 72, 4791 (1950). Kazanskii and Lukina, Doklady Akad. Nauk S.S.S.R., 83, 693 (1952) [C. A., 47, 2712)

141 Bischoff and von Kuhlberg, Ber., 23, 634 (1890).

142 Bischoff and Mintz, Ber., 23, 647 (1890). 141 Auwers and Jackson, Ber., 23, 1599 (1890).

144 Zelinsky and Bestedka, Ber., 24, 459 (1891).

161 Bischoff, Ber., 24, 1041 (1891).

166 Auwers and Kohner, Ber., 24, 1923 (1891).

16: Bone and Sprankling, J. Chem. Soc., 75, 839 (1899). 144 Emery, J. prakt. Chem., [2] 53, 308 (1896).

Decarbalkoxylation (p. 127) and side reactions which involve the alkylating agent and the base may be minimized if a mixture of the alkylating agent and the active methylene compound is treated with the base at a rate equal to that at which the base is consumed in the reaction. 42,121,169,170

Similarly, the slow addition of the sodium derivatives of mononitriles to allylie halides has been found to minimize the extent of polymerization of both the alkylating agent and the product.<sup>171</sup>

Certain vicinal dihalides tend to lose their halogen atoms with the simultaneous production of the corresponding olefin under the conditions of the alkylation reaction. Such dihalides include ethylene iodide (but not ethylene bromide), 92 2,3-dibromo-2-methylbutane, 172,173 0,0'-dinitrostilbene dibromide, 174 and diethyl erythro- $\alpha$ , $\alpha'$ -dibromosuccinate. For each molecule of halogen lost, two molecules of the active methylene compound are coupled in a reaction similar to the coupling of active methylene compounds in the presence of iodine (p. 137). Certain of the olefins produced in this way may add an additional equivalent of the active methylene compound in a Michael reaction. The reaction of

dimethyl erythro-α,α'-dibromosuccinate is illustrative. In addition to the major products, dimethyl fumarate, tetramethyl 1,1,2,2-ethanetetra-carboxylate, and tetramethyl 1,1,2,3-propanetetracarboxylate, a small amount of racemic tetramethyl 1,1,2,3-cyclopropanetetracarboxylate was formed. The eyclopropane tetracarboxylic ester is believed to arise from

<sup>169</sup> Phillips, Ind. Chemist, 21, 678 (1945).

<sup>170</sup> Mariella and Raube, Org. Syntheses, 33, 23 (1953).

<sup>171</sup> Whyte and Cope, J. Am. Chem. Soc., 65, 1999 (1943).

<sup>171</sup> Bischoff, Ber., 28, 2824 (1895).

<sup>173</sup> Ipation, J. Russ. Phys. Chem. Soc., 30, 391 (1898) (Chem. Zentr., 1898, 11, 660).

<sup>174</sup> Bischoff, Ber., 21, 2071 (1888).

<sup>175</sup> Ing and Perkin, J. Chem. Soc., 125, 1814 (1924).

the partial base-catalyzed isomerization of the dimethyl  $erythro.\alpha,\alpha'$  dibromosuccinate to the threo isomer; dimethyl  $threo.\alpha,\alpha'$ -dibromosuccinate, when treated with dimethyl sodiomalonate, was converted to

the racemic cyclopropane tetracarboxylie ester in 80–90% yield. In similar base-catalyzed epimerization of the isomerie  $\alpha,\alpha'$ -dibromoglutaric esters has been observed. In 6

Another side reaction which involves the transfer of a halogen atom is exemplified by the attempted alkylation of methyl diphenylacetate with methyl  $\alpha$ -bromophenylacetate in the presence of sodium triphenylmethide. The product was dimethyl  $\alpha,\alpha'$ -diphenylsuccinate.

Similarly, 2-bromo-2-nitropropane and diethyl sodiomalonate underwent partial halogen interchange, the products being tetraethyl 1,1,2,2-cthanetetracarboxylate and 2,3-dimethyl-2,3-dinitrobutane. However, normal alkylation was observed when 2-chloro-2-nitropropane was allowed to react with the sodium enolate of diethyl cthylmalonate. Halogenated nitroalkanes in which the nitro group is bonded to a carbon atom

bearing a hydrogen atom cannot be employed as alkylating agents. Instead, the enolate of the nitro compound is formed, since it is less basic than the enolate of malonie ester

In addition to the side reactions that can occur with the alkylating agent, both the initial active methylene compound and the alkylated product can undergo a number of transformations. The possibility of ester interchange when the alkoxyl group of the ester and the alkoxide ion differ has already been mentioned (p. 117). When sodium amide is

Ing and Perkin, J. Chem. Soc., 127, 2387 (1925).
 New Tenselen and Van Zyl, J. Am. Chem. Soc., 71, 835 (1949).

used as the base for the alkylation of esters, amide formation may be z serious side reaction.  $^{178,179}$ 

$$\mathbf{C_5H_5CH_2CO_2C_2H_5} + \mathbf{H_2N^{\odot}} \rightleftarrows \mathbf{C_5H_5CH_2C} \\ \mathbf{C_6H_5CH_2CONH_2} + \mathbf{C_2E_5C^{\circ}} \\ \mathbf{NH_2}$$

A related side reaction results in the loss of the carbalkoxyl group as the corresponding dialkyl carbonate. Similarly, cyanoacetic esters are converted to mononitriles. Among the malonic esters the importance

$$\begin{array}{c} C_6H_5CH(CO_2C_2H_5)_2 & \xrightarrow{C_2H_5O} \\ \hline \\ C_6H_5CH(CO_2C_2H_5)_2 & \xrightarrow{C_2H_5O} \\ \hline \\ C_5H_5CHCO_2C_2H_5 + (C_2H_5O)_2CO \\ \hline \\ C(CH_3)(CN)CO_2C_2H_5 + C_2H_5O \\ \hline \\ \hline \\ C_6CH_5CHCO_2C_2H_5 + (C_2H_5O)_2CO \\ \hline \\ \hline \\ C_6CH_3CHCO_2C_2H_5 + (C_2H_5O)_2CO \\ \hline \\ C_6CH_5CHCO_2C_2H_5 + (C_2H_5O)_2CO \\ \hline \\ C_6CH_5CHCO_2C_2H_5$$

of this side reaction decreases in the following order: diethyl diphenylmalonate > diethyl ethyl(phenyl)malonate > diethyl diethylmalonate. 150

$$(C_{6}H_{5})_{2}C(CO_{2}C_{2}H_{5})CO_{2}H_{5} \longrightarrow (C_{2}H_{5}O)_{2}CO \div$$

$$C_{2}H_{5} \longrightarrow C_{2}H_{5} \longrightarrow C_{2}H_{5}OO_{2}H_{5} \longrightarrow C_{2}OO_{2}H_{5}$$

Such an order is understandable when the resonance stabilization available to the carbanion formed after loss of diethyl carbonate is considered. Substituents other than the phenyl group 180,182 which have been observed to enhance the eleavage reaction include the nitro group,183 the vinyl group,54 the 2,4-dinitrophenyl group,184 and the 2- or 3-indenyl group.181 On the other hand, bulky groups that impede the approach of the ethoxide ion or substituents that reduce the stability of a earbanion diminish the amount of decarbethoxylation. Malonic esters and monoalkylmalonic esters are less readily eleaved to monocarboxylic esters and dialkyl earbonates because they react readily with sodium alkoxides to form stable enolates.

The reversible nature of the decarbethoxylation of diethyl phenylmalonate has been demonstrated.43 In fact, the reverse reaction, earbethoxylation, has been found valuable both in the synthesis of diethyl phenylmalonate from ethyl phenylacetate and in the synthesis of eyanoacetic esters from mononitriles. 185-189 As mentioned previously (p. 117), the use of diethyl earbonate as a solvent for the alkylation reaction offers special advantages where cleavage might be an important side reaction. The extent of decarbethoxylation is diminished and the reaction time is shortened by virtue of the high boiling point of the diethyl earbonate.

The decarbethoxylation of disubstituted malonic esters at high temperatures in the presence of ethanol-free sodium ethoxide or sodium or potassium metal (p. 150) would constitute a serious side reaction where the alkylation of an alkylmalonic ester was attempted under such conditions.

In the alkylation of malononitriles (see Table X), the addition of ethanol to one of the eyano groups to produce stable imido esters is often observed. 95,104 The mononitriles are usually stable to ethanolic sodium

$$\begin{array}{c} {\rm C_6H_5CH_2CH(CN)_2+CH_3I+C_2H_5OH} \xrightarrow{\rm NaOC_2H_5} \\ {\rm C_6H_5CH_2C(CH_3)(CN)COC_2H_5} \\ {\rm NH} \end{array}$$

cthoxide, 4-cyano-1-methyl-4-phenylpiperidine being an exception; 190 an imido ester presumably is an intermediate in the cleavage. The stronger base, sodium amide, does attack the cyano group in such solvents as boiling benzene,<sup>191</sup> toluene,<sup>192</sup> or xylene.<sup>191–194</sup> Under such conditions

$$\begin{array}{c|c} H_3CN & \xrightarrow{C_6H_5} & \xrightarrow{C_2H_5OH, \ NaOC_2H_5} & H_3CN & \\ \hline C = N & & & & \\ \end{array}$$

the nitrile function may be eliminated as sodium cyanamide.

$$(C_6H_5)_2C(CN)CH_2CH_2N(CH_3)_2 + 2NaNH_2 \xrightarrow{Xylene}$$
 
$$NH_3 + Na_2N_2C + (C_6H_5)_2CHCH_2CH_2N(CH_3)_2$$
 91%

The loss of the nitrile function has also been observed with substituted nitriles which have no hydrogen atom on the carbon atom alpha to the nitrile group and which have a hydrogen atom and a phenyl group on the carbon atom beta to the eyano group. This elimination of hydrogen cyanide may be likened to other bimolecular elimination processes as is shown in the accompanying equation. In the presence of basic catalysts

$$\begin{array}{c} & \overset{\circ}{\text{N}}\text{H}_2 \\ & \overset{\circ}{\text{H}} \\ \text{C}_6\text{H}_5\text{CH} \overset{\circ}{\text{-C}}\text{(C}_6\text{H}_5)_2 \rightarrow \text{C}_6\text{H}_5\text{CH} \overset{\circ}{\text{--C}}\text{(C}_6\text{H}_5)_2 + \text{NH}_3 + \text{CN}} \\ & & \overset{\circ}{\text{-C}}\text{N} \end{array}$$

both acetic esters and mono- and di-substituted acetic esters can condense with themselves in a reaction of the acetoacetic ester type<sup>179</sup> to produce  $\beta$ -keto esters with a consequent diminished yield of the alkylated product.<sup>178,196</sup> A similar condensation, the Thorpe reaction, occurs as a side reaction and results in poor yields in the alkylation of certain mono-nitriles.<sup>71–73</sup> Such Claisen-type condensations become particularly important with compounds where intransolcular condensation is possible.<sup>176,197–201</sup> The accompanying example<sup>198</sup> illustrates both a

- 191 Ruddy, J. Am. Chem. Soc., 73, 4096 (1951).
- <sup>182</sup> Jackman, Nachod, and Archer, J. Am. Chem. Soc., 72, 716 (1950).
- <sup>193</sup> Jackman, Bolen, Nachod, Tullar, and Archer, J. Am. Chem. Soc., 71, 2301 (1949).
- <sup>194</sup> Kleiderer, Report No. P.B. 981, Office of the Publication Board, Dept. of Commerce, Washington, D.C.
  - 195 Hauser and Brasen, to be published.
  - 196 Scheibler, Marhenkel, and Bassanoff, Ber., 58, 1198 (1925).
  - 197 Perkin and Thorpe, J. Chem. Soc., 79, 729 (1901).
  - 198 Mitchell and Thorpe, J. Chem. Soc., 97, 2261 (1910).
  - 199 Goss and Ingold, J. Chem. Soc., 1928, 1268.
  - <sup>122</sup> Acheson and Robinson, J. Chem. Soc., 1952, 1127.
  - <sup>201</sup> Kierstend, Linstend, and Weedon, J. Chem. Soc., 1953, 1799.

Claisen condensation and the subsequent elimination of a carbethoxyl group.

$$\begin{array}{c|c} CH_2 \\ CH(CO_2C_2H_5)_2 & \xrightarrow{NaOC_2H_5} \\ CN & & NH \end{array}$$

Active methylenc compounds having  $alkoxyl^{202-204}$  or  $alkylthio^{205}$ functions bonded to the carbon atom beta to the activating group have been observed to undergo base-catalyzed elimination under the conditions of the alkylation reaction. The unsaturated compounds initially formed are susceptible to polymerization and Michael reactions.

During the alkylation of certain malonic esters a reverse Michael reaction competes with the alkylation reaction. In such eases the alkylation products of diethyl malonate or diethyl monoalkylmalonates are isolated. 87,154,206,207 For example, the products of the alkylation of ethyl  $\gamma$ -benzoyl- $\alpha$ -carbethoxy- $\beta$ -phenylbutyrate (I) were dependent on the alkylating agent employed.154 With methyl iodide both the keto

<sup>&</sup>lt;sup>202</sup> Ziegler, Schenck, Krockow, Siebert, Wenz, and Weber, Ann., 551, 1 (1942).

<sup>&</sup>lt;sup>203</sup> McElvain and Burkett, J. Am. Chem. Soc., 64, 1831 (1942).

<sup>&</sup>lt;sup>204</sup> Simonsen, J. Chem. Soc., 93, 1777 (1908).

<sup>205</sup> Böhme and Greve, Chem. Ber., 85, 409 (1952).

<sup>206</sup> Perkin, J. Chem. Soc., 69, 1500 (1896).

<sup>207</sup> Rydon, J. Chem. Soc., 1935, 420.

ester II (R = CH<sub>3</sub>) and diethyl methylmalonate (III, R = CH<sub>3</sub>) were formed. If the less reactive ethyl iodide was employed, only diethyl ethylmalonate (III, R = C<sub>2</sub>H<sub>5</sub>) was produced since the reaction mixture remained basic sufficiently long for the reverse Michael reaction to predominate. Whether the cleavage occurred before or after the alkylation step is not known.

If the active methylene compound employed contains other reactive functions additional side reactions are possible. In the case of diethyl chloromalonate the rate of displacement of the chloride ion by the ethoxide anion exceeds the rate of alkylation except with very reactive alkylating agents such as benzyl chloride<sup>208</sup> or 4-(or 5-)chloromethylimidazole.<sup>209</sup> Small amounts (1.5%) of diethyl 5-ethoxyhexylmalonate were formed along with diethyl 2-methylcyclohexane-1,1-dicarboxylate when diethyl 5-bromohexylmalonate was cyclized in the presence of sodium ethoxide.<sup>210</sup>

Additional side reactions may accompany the alkylation of alkylidenemalonic esters, alkylidenecyanoacetic esters, and alkylidenemalononitriles. These include polymerization<sup>28,37,211,212</sup> and reverse aldol reactions.<sup>28</sup> If sodium in an inert solvent is used to prepare the enolates of alkylidene esters partial reduction may occur (p. 119).

The products obtained from the alkylation of alkylidene derivatives of malonic ester, <sup>64</sup>, <sup>213</sup> cyanoacetic ester, <sup>64</sup>, <sup>214</sup> malononitriles, <sup>215</sup>, <sup>216</sup> and mononitriles<sup>171</sup> with allylic halides have been found to undergo thermal isomerization in certain cases, and the products must be distilled at temperatures that do not cause rearrangement. For the various active methylene compounds used, the rates of such rearrangements fall in the order: malononitriles > cyanoacetic esters > malonic esters. <sup>171</sup>, <sup>213</sup>, <sup>215</sup>, <sup>216</sup>

$$\begin{array}{ccccc} \mathrm{CH}_2 \!\!=\!\! \mathrm{C-CH}_3 \\ & & & & \mathrm{C(CO}_2\mathrm{C}_2\mathrm{H}_5)_2 \xrightarrow{185^\circ} & \mathrm{CH}_2 \!\!-\!\! \mathrm{CCH}_3 \\ & & & & & & & & & \\ \mathrm{CH}_3\mathrm{CH} \!\!=\!\! \mathrm{CHCH}_2 & & & & & & \\ & & & & & & & & \\ \mathrm{CH}_3\mathrm{CH} \!\!-\!\! \mathrm{CH}_2\mathrm{CH}_2 \\ & & & & & & & \\ \end{array}$$

Steric effects influence markedly the ease of these rearrangements.<sup>213</sup>,<sup>215</sup>

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<sup>208</sup> Conrad, Ann., 209, 241 (1881).
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<sup>&</sup>lt;sup>209</sup> Pyman, J. Chem. Soc., 99, 1386 (1911).

<sup>&</sup>lt;sup>210</sup> Gol'mov, Zhur. Obshchel Khim. (J. Gen. Chem. U.S.S.R.), 23, 1162 (1953) [C. A., 47, 12255 (1953)].

<sup>&</sup>lt;sup>211</sup> Cope and Hoyle, J. Am. Chem. Soc., 63, 733 (1941).

<sup>&</sup>lt;sup>212</sup> Cope, U.S. pat. 2,222,455 [C. A., 35, 1802 (1941)].

<sup>&</sup>lt;sup>213</sup> Aldridge and Murphy, J. Am. Chem. Soc., 73, 1158 (1951).

<sup>&</sup>lt;sup>214</sup> Cope and Hardy, J. Am. Chem. Soc., 62, 441 (1940).

<sup>&</sup>lt;sup>215</sup> Cope, Hoyle, and Heyl, J. Am. Chem. Soc., 63, 1843 (1941).

<sup>&</sup>lt;sup>216</sup> Foster, Cope, and Daniels, J. Am. Chem. Soc., 69, 1893 (1947).

<sup>&</sup>lt;sup>217</sup> Cope and Field, J. Am. Chem. Soc., 71, 1589 (1949).

## The Active Methylene Compound

Malonic Esters (Table I). In the many alkylations reported to yield monoalkylmalonic esters, the base-solvent combination generally employed was sodium ethoxide in ethanol. As noted previously (p. 120) such reaction conditions inhibit dialkylation since, in most cases, the monoalkyl derivative is less acidic than ethanol. This advantage, which is not shared with cyanoacetic ester and malononitrile, recommends malonic ester if only the monoalkyl compound is desired. The separation problem that arises in the preparation of methylmalonic esters and ethylmalonic esters (p. 123) is best avoided by employing an alternative synthetic method (p. 147) for these esters. The use of the ethoxymagnesium salt of malonic ester rather than sodiomalonic ester is a valuable modification 55,56,150,218-220 if the alkylation is to be run in an inert solvent such as ether or benzene (p. 116). Diethyl carbonate (pp. 117, 128) offers advantages as the solvent in some instances.

Substituted Malonic Esters (Tables II, III, and IV) and Alkylidenemalonic Esters (Table V). The reduced acidity of monoalkylmalonic esters (p. 110) in which the alkyl group is secondary or tertiary 44,52,145-149,221-226 has resulted in low yields during alkylations in the presence of ethanolic sodium ethoxide. This difficulty, which is much less serious with the analogous cyanoacetic esters (p. 134), has been overcome by recourse to stronger bases and less acidic solvents. The use of sodium t-butoxide in t-butyl alcohol has permitted the alkylation of diethyl isopropylmalonate, 35 diethyl (1-ethylbntyl)malonate, 35 and diethyl eyelohexylmalonate.35 Diethyl diisopropylmalonate was prepared by the use of sodium and ether at elevated temperatures in a sealed tube. 52 Diethyl ethyl-(sec-butyl)malonate was obtained in 95% yield when the ethanolfree sodium enolate of diethyl sec-butylmalonate was heated with chyl bromide in diethyl carbonate. 44,51,227 Another striking demonstration of the value of this method is found in the alkylation of diethyl t-butylmalonate with allyl bromide, the reaction being effected in 36% yield in the presence of sodium ethoxide and diethyl carbonate.44 Benzene and tolnene have

<sup>&</sup>lt;sup>218</sup> Fuson and Jackson, J. Am. Chem. Soc., 72, 351 (1950). <sup>219</sup> Ali-Zade and Arbuzov, Zhur. Obshchel Khim. (J. Gen. Chem. U.S.S.R.), 13, 113 (1943) [C. A., 38, 352 (1944)].

<sup>220</sup> Terent'ev, J. Russ. Phys. Chem. Soc., 60, 85 (1928) [C. A., 22, 3880 (1928)]. <sup>221</sup> Conrad and Guthzeit, Ann., 222, 249 (1883).

<sup>222</sup> Fischer and Dilthey, Ann., 335, 334 (1904).

<sup>223</sup> Bischoff, Ber., 29, 972 (1896).

<sup>&</sup>lt;sup>221</sup> Cope and Lyman, J. Am. Chem. Soc., 75, 3312 (1953).

<sup>225</sup> Marshall, J. Chem. Soc., 1930, 2754.

<sup>226</sup> Weizmann, Sulzbacher, and Bergmann, J. Chem. Soc., 1947, 772. <sup>227</sup> Wallingford and Homeyer, U.S. pat. 2,391,530 [C. A., 40, 3770 (1946)].

served as solvents for the alkylation of the sodium salts of diethyl benz-hydrylmalonate<sup>156</sup> and dibenzhydryl benzhydrylmalonate<sup>224</sup> with benzhydryl bromide.

The introduction of a phenyl group reduces the acidity of diethyl malonate or ethyl phenylacetate, the reduction in acidity being comparable with that resulting from the introduction of a methyl group (p. 110).<sup>5</sup> An explanation for this phenomenon may be the non-coplanarity of the phenyl derivative, which inhibits effective resonance stabilization of the enolate anion.

Alkylation of chloromalonic ester is successful only with very reactive alkylating agents (p. 131).209,228-230 With less reactive alkylating agents, coupling of the malonic ester residues<sup>231</sup> or ether formation is the predominant reaction. In the alkylation of nitromalonic ester, the alkyl group is introduced on the earbon atom<sup>183</sup> rather than on an oxygen atom. Whereas the alkylation of aminomalonic esters results in both C- and N-alkylation, 232 formamido, acetamido, benzamido, and phthalimido derivatives of malonic ester can be alkylated without N-alkylation. The formamido- and acetamido-malonates are most useful since the phthalimido derivatives are hydrolyzed and decarboxylated with difficulty<sup>233</sup> and many of the alkyl(benzamido)malonic esters are oils.<sup>232</sup> The facile deacylation of formamidomalonates and acetamidomalonates may be disadvantageous if the alkylation reaction is slow. The yields of the isopropyl derivative obtained with diethyl acetamidomalonate (37%)<sup>234</sup>,<sup>235</sup> and with diethyl benzamidomalonate (66%)<sup>233</sup> are explicable in terms of the greater susceptibility of the acetamido group to alcoholysis. The absence of alcohol in the reaction mixture has proved advantageous in the alkylation of diethyl phthalimidomalonate with 1,3-dibromopropane and with  $\gamma$ -phthalimidopropyl bromide.<sup>236</sup>

The alkylation of alkylidenemalonic esters produces the  $\alpha$ -alkyl derivative of the corresponding  $\beta$ ,  $\gamma$ -unsaturated ester. The accompanying

$$\begin{array}{c} \text{CH}_3\text{CH}_2\text{C(CH}_3) \!\!=\!\! \text{C(CO}_2\text{C}_2\text{H}_5)_2 + n \cdot \text{C}_3\text{H}_7\text{Br} \xrightarrow{\text{NaNH}_2} \\ \text{CH}_3\text{CH} \!\!=\!\! \text{C(CH}_3)\text{C}(n \cdot \text{C}_3\text{H}_7)(\text{CO}_2\text{C}_2\text{H}_5)_2 \end{array}$$

example  $^{237}$  illustrates the shift of the double bond to yield the more highly

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<sup>228</sup> Perkin, J. Chem. Soc., 53, 1 (1888).
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<sup>&</sup>lt;sup>229</sup> Kipping, J. Chem. Soc., 53, 21 (1888).

<sup>&</sup>lt;sup>230</sup> Titley, J. Chem. Soc., 1928, 2571.

<sup>&</sup>lt;sup>231</sup> Kötz and Zörnig, J. prakt. Chem., [2] 74, 425 (1906).

<sup>&</sup>lt;sup>232</sup> Albertson, J. Am. Chem. Soc., 68, 450 (1946).

<sup>&</sup>lt;sup>233</sup> Redemann and Dunn, J. Biol. Chem., 130, 341 (1939).

<sup>&</sup>lt;sup>234</sup> Atkinson and Scott, J. Chem. Soc., 1949, 1040.

<sup>&</sup>lt;sup>235</sup> Snyder, Shekleton, and Lewis, J. Am. Chem. Soc., 67, 310 (1945).

<sup>&</sup>lt;sup>236</sup> Sörensen, Hoppe Seyler's Z. physiol. Chem., 44, 448 (1905).

<sup>&</sup>lt;sup>237</sup> Cope and Hancock, J. Am. Chem. Soc., 60, 2901 (1938).

substituted vinyl derivative, which occurs when the double bond can migrate into either of two positions. As with saturated alkylmalonic ester derivatives, chain branching markedly reduces the acidity of alkylidenemalonic esters. Although sodium ethoxide may serve as the base for the alkylation of alkylidenemalonic esters derived from aldehydes,<sup>28</sup> the branched alkylidene derivatives prepared from ketones require a stronger base.<sup>237</sup> Since the use of sodium in an inert solvent causes reduction of the alkylidene derivative (p. 119), sodium amide in liquid ammonia or in an inert solvent has proved to be most satisfactory for the preparation of enolates from alkylidenemalonic esters derived from ketones.

Cyanoacetic Esters (Table VI). Like malonie esters, cyanoacetic esters are usually alkylated in the presence of ethanolic sodium ethoxide. The increased importance of dialkylation (p. 121) as a side reaction attending the alkylation of cyanoacetic esters has been discussed. The high order of reactivity of the ethyl cyanoacetate enolate has been utilized advantageously to prevent side reactions with very reactive alkylating agents;<sup>238</sup> in such cases reaction of the alkylating agent with the enolate anion is apparently more rapid than the reaction of the alkylating agent with the base or the solvent.

Substituted Cyanoacetic Esters (Tables VII and VIII) and Alkylidenecyanoacetic Esters (Table IX). The use of eyanoacetic esters rather than malonic esters is recommended if the preparation of a dialkyl derivative is desired. Monoalkyl derivatives of eyanoacetic ester arc readily alkylated in the presence of ethanol and sodium ethoxide even if the first alkyl group introduced is branched. 145,225,226,238-240 This property both simplifies the preparation of dialkylcyanoacetic esters and eliminates the need to introduce the primary alkyl group in the first stage of the alkylation as often must be done with malonic esters (p. 123). For example, ethyl ethyl(isopropyl)cyanoacetate was prepared in 86% yield from ethyl isopropyleyanoacetate and ethyl iodide, 239 whereas diethyl ethyl(isopropyl)malonate was obtained from diethyl isopropylmalonate under similar conditions in very poor yield. 145

Ethyl acetamidocyanoacetate<sup>232</sup>, <sup>241</sup>, <sup>242</sup> and methyl (phenylacetamido)cyanoacetate<sup>243–245</sup> have been alkylated in the presence of alcoholic

Tabern and Volwiler, J. Am. Chem. Soc., 56, 1139 (1934).
 Fischer, Robdo, and P.

Fischer, Rohde, and Brauns, Ann., 402, 364 (1914).
 Fischer and Flatau, Ber., 42, 2981 (1909).

Albertson and Tullar, J. Am. Chem. Soc., 67, 502 (1945).
 Fields, Walz and Path. J. J.

 <sup>242</sup> Fields, Walz, and Rothchild, J. Am. Chem. Soc., 73, 1000 (1951).
 243 Ehrhart, Chem. Ber., 82, 60 (1949).

<sup>244</sup> Ehrhart, Chem. Ber., 82, 387 (1949).

<sup>245</sup> Horner and Medem. Chem. Ber., 85, 520 (1952).

sodium alkoxides without difficulty. Sodium hydride has been recommended as the base for the alkylation of acetamidomalonic ester and acetamidoeyanoacetie ester.246

The alkylation of alkylideneeyanoacetic esters derived from aldehydes has failed because these alkylidene derivatives are rapidly polymerized in the presence of bases.212 Aside from the fact that only the alkylidenemalonie esters derived from the simplest ketones are available, 37,74 the use of alkylidenceyanoacetic esters derived from ketones rather than the malonie ester analogs offers an advantage in that the cyanoacetate derivatives may be alkylated in the presence of ethanolic sodium ethoxide.37 However, sodium isopropoxide in isopropyl alcohol has been recommended for the alkylation of secondary alkylidenecyanoacetic esters. 37,211,247

Malononitriles (Table and Alkylidenemalononitriles X) (Table IX). Malononitrile, monoalkylmalononitriles, and alkylidenemalononitriles have been alkylated in the presence of ethanolie sodium ethoxide. However, the usefulness of the reaction is often limited by the simultaneous addition of the aleohol to one of the nitrile groups of the product<sup>95,104,211</sup> to produce an imido ester (p. 128). In addition the alkylidenemalononitriles derived from aldehydes polymerize very readily.<sup>211</sup> The use of malononitrile to form monoalkyl derivatives is limited by the ease with which it is dialkylated.95

Monocarboxylic Esters (Table XI), 3-Aryl-2-benzofuranones (Table XII), and Succinic, Glutaric and Glutaconic Esters (Table XIII). Either sodium anide or sodium triphenylmethide in an inert solvent is the base most often used to produce the enolates of monocarboxylic esters. These sodium enolates have been alkylated with alkyl and allyl halides, with dihalogenated alkanes,248 with phenacyl bromide,248 with nairces, with amanagement and property of the posides, of with epoxides, of with dialkyl sulfates,<sup>249</sup> and with alkyl sulfonates.<sup>69</sup> In contrast to the mononitriles (p. 136), dialkylation is not a serious problem. The 3-aryl-2benzofuranones most often have been alkylated by treatment with sodium or potassium metal in an inert solvent followed by treatment with an or potassium metal in an increase of the solution with an alkylating agent. Several α-bromoglutaric esters have been converted to alkylating agent. Several a-browneg. the corresponding cyclopropane derivatives by self-alkylation, the base used being sodium carbonate or potassium hydroxide. 80,250

As cited previously (p. 110), the acidity of acetic esters is reduced by As cited previously (p. 110), the askyl group is branched, s alkyl substitution especially if the alkyl group is branched, s Although the alkyl substitution especially in the acidity of ethyl acetate is enhanced by the substitution of one phenyl group

<sup>&</sup>lt;sup>246</sup> Shapira, Shapira, and Dittmer, J. Am. Chem. Soc., 75, 3655 (1953) <sup>247</sup> Mitter and Dutta, J. Indian Chem. Soc., 25, 306 (1948).

<sup>248</sup> Wislicenus and Mocker, Ber., 46, 2772 (1913).

<sup>219</sup> Bowden, J. Am. Chem. Soc., 60, 131 (1938).

<sup>&</sup>lt;sup>250</sup> Perkin and Thorpe, J. Chem. Soc., 75, 48 (1899).

of the base potassium amide in a mixture of liquid ammonia and ether as the solvent has proved advantageous for the alkylation of phenylaeetonitrile and diphenylaeetonitrile. The alkylating agents employed include alkyl and allyl halides, dihalogenated alkanes, chloropyridines, chloroquinolines, epoxides, dialkyl sulfates, and alkyl sulfonates. In some instances elevated reaction temperatures favor dialkylation, <sup>53</sup> elimination of the cyano group, <sup>91,191–193</sup> or dimerization of the nitrile. <sup>71–73</sup> When 2- or 4-chloropyridines or 4-chloroquinolines were employed as the alkylating agent for phenylaeetonitrile the yield of product did not exceed 50% unless two equivalents of sodium amide were used. <sup>178,254</sup> This result has been attributed to the formation of an insoluble sodium salt which removed an additional equivalent of base from the reaction mixture. <sup>178</sup>

The metal salts of primary and secondary amines have been used as bases for the alkylation of mononitriles.<sup>53,66,255</sup> Sodium hydroxide and potassium hydroxide have also served as bases for the alkylation of nitriles.<sup>34,75-79,256,257</sup>

$$C_{6}H_{5}\overset{\circ}{\text{CHCN}}\text{Na}\oplus + C_{\text{Cl}}\overset{C_{1}}{\longrightarrow} \text{NaCl} + C_{\text{Cl}}\overset{C_{6}H_{5}\text{CHCN}}{\longrightarrow} \text{C}_{6}H_{5}\overset{\circ}{\text{CHCN}} \text{Na}\oplus + C_{\text{Cl}}\overset{C_{6}H_{5}\text{CHCN}}{\longrightarrow} \text{C}_{6}H_{5}\overset{\circ}{\text{CH}_{2}\text{CN}} + C_{\text{Cl}}\overset{C_{6}H_{5}\text{CHCN}}{\longrightarrow} \text{Na}\oplus + C_{\text{Cl}}\overset{\circ}{\longrightarrow} \text{C}_{6}H_{5}\overset{\circ}{\text{CH}_{2}\text{CN}} + C_{\text{Cl}}\overset{\circ}{\longrightarrow} \text{Na}\oplus + C_{\text{C$$

Aldehydes<sup>258,259</sup> and ketones<sup>171,193,259</sup> condense readily with mononitriles. The alkylidene derivatives formed from ketones are best converted to their sodium enolates with sodium amide. Thus the alkylation of cyclohexylidene(phenyl)acetonitrile failed in ethanolic sodium ethoxide;<sup>259</sup> with the stronger base sodium amide in benzene or ether, alkylated products were obtained in yields of 77–82%.<sup>171</sup>

## Alkylating Agents

Halogens. The addition of bromine or iodine to an enolate often results in the coupling of two molecules of the active methylene compound. The

<sup>&</sup>lt;sup>254</sup> Sperber, Papa, Schwenk, Sherlock, and Fricano, J. Am. Chem. Soc., 73, 5752 (1951).

<sup>&</sup>lt;sup>255</sup> Ziegler, Ger. pat. 583,561 [C. A., 28, 1057 (1934)].

<sup>&</sup>lt;sup>256</sup> Meyer, Ann., 250, 118 (1888).

<sup>&</sup>lt;sup>257</sup> Haller and Benoist, Ann. chim. Paris, [9] 17, 25 (1922).

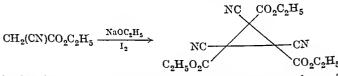
<sup>&</sup>lt;sup>258</sup> Murray and Cloke, J. Am. Chem. Soc., 58, 2014 (1936).

<sup>&</sup>lt;sup>259</sup> McRae and Manske, J. Chem. Soc., 1928, 484.

probable course of the reaction  $^{107,260,261}$  will be seen to resemble the course of an analogous side reaction involving vicinal dihalides (p. 125). Similar dimeric products have been formed from monocarboxylic esters,  $^{67,69,248}$  3-aryl-2-benzo-furanones,  $^{262,263}$  and mononitriles.  $^{264}$  However, the enolates of some monosubstituted malonic esters formed only the iodinated derivative of the active methylene compound when treated with iodine.  $^{265}$  That monosubstitution need not always inhibit this coupling reaction is indicated by the treatment of various polymethylene- $\alpha$ , $\omega$ -dimalonic esters with iodine and a base; the corresponding carbocycles are formed.  $^{87,266-269}$ 

$$\begin{array}{c} {\rm C_2H_5CH[CH(CO_2C_2H_5)_2]_2 + 2NaOC_2H_5 + I_2 \rightarrow} \\ {\rm H_5C_2CH} & + 2NaI + 2C_2H_5OH \\ {\rm C(CO_2C_2H_5)_2} \end{array}$$

When the sodium enolate of ethyl cyanoacetate is treated with iodine a cyclic trimer is formed;<sup>270-272</sup> the same product results when ethyl bromocyanoacetate is heated with aniline in ether.<sup>273</sup>



Alkyl Halides. In reactivity as alkylating agents for active methylene compounds the various halogenated organic compounds lie in the order observed for other bimolecular nucleophilic displacement reactions; the allyl and benzyl halides are more reactive than the alkyl halides,<sup>274</sup> which in turn are more reactive than the vinyl<sup>54</sup>,<sup>275</sup>–<sup>277</sup> and aryl<sup>142</sup>,<sup>278</sup> halides.

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261 Lennon and Perkin, J. Chem. Soc., 1928, 1513.
<sup>262</sup> Löwenbein and Simonis, Ber., 57, 2040 (1924).
<sup>263</sup> Löwenbein, Ber., 58, 601 (1925).
<sup>264</sup> Auwers and Meyer, Ber., 22, 1227 (1889).
<sup>265</sup> Bischoff and Hausdörfer, Ann., 239, 110 (1887).
266 Perkin, J. Chem. Soc., 51, 1 (1887).
 267 Perkin, J. Chem. Soc., 51, 240 (1887).
 268 Perkin, J. Chem. Soc., 65, 572 (1894).
 269 Haworth and Perkin, J. Chem. Soc., 65, 591 (1894).
 270 Errera and Perciabosco, Ber., 33, 2976 (1900).
 <sup>271</sup> Engler and Meyer, Ber., 38, 2486 (1905).
 272 Thorpe and Young, J. Chem. Soc., 77, 937 (1900).
  273 Goldthwaite, Am. Chem. J., 30, 447 (1903).
  <sup>274</sup> Noller and Adams, J. Am. Chem. Soc., 48, 2444 (1926).
  <sup>275</sup> Benary and Schinkopf, Ber., 56, 354 (1923).
  <sup>276</sup> V. Voorhees, Ph.D. Dissertation, University of Wisconsin, 1924.
  <sup>277</sup> Heyl and Cope, J. Am. Chem. Soc., 65, 669 (1943).
  <sup>278</sup> Dox and Thomas, J. Am. Chem. Soc., 45, 1811 (1923).
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260 Bischoff and Rach, Ber., 17, 2781 (1884).

Likewise, for a given alkyl group the iodide is more reactive than the bromide, <sup>34</sup>, <sup>37</sup>, <sup>40</sup>, <sup>142</sup>, <sup>234</sup>, <sup>279</sup>–<sup>281</sup> which is more reactive than the chloride, <sup>282</sup>–<sup>284</sup> the fluoride being almost inert. <sup>285</sup> Since very reactive halogen compounds favor dialkylation (p. 121), it is usually advisable to select the least reactive halide as an alkylating agent where dialkylation is expected to be a serious side reaction. <sup>140</sup>, <sup>280</sup>

Alkyl halides that are readily dehydrollalogenated (e.g., tertiary alkyl halides) are unsuitable alkylating agents (p. 124), since the yield of alkylated product is materially reduced by the loss of both base and alkyl halide which accompanies dehydrollalogenation.<sup>44,149,168,286</sup> For example, one-third of the cyclohexyl bromide employed in the alkylation of diethyl malonate was converted to cyclohexene.<sup>286</sup>

Although the alkyl bromides are usually the most satisfactory alkylating agents, the alkyl chloride is recommended when the corresponding alkyl bromide is very reactive. If the alkyl bromide is relatively unreactive, use of the corresponding alkyl iodide is preferable. If the desired alkyl iodide is not available a satisfactory alternative employs mixtures of the alkyl bromide or alkyl chloride with sodium iodide<sup>70</sup>,287-289,291 or potassium iodide<sup>290</sup>,292 in alcoholic media.

Di- and Poly-halides. Alkylation reactions involving methylene ehloride,<sup>293,294</sup> methylene bromide,<sup>295</sup> and methylene iodide<sup>296-300</sup> have been found to proceed normally. Such dihalides have been especially valuable for the preparation of cyclic systems.<sup>296,299-302</sup> However, a <sup>279</sup> Rossolymo, Ber., 22, 1233 (1889).

280 Bischoff, Ber., 28, 2616 (1895).

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<sup>281</sup> Kuhn, Köhler, and Köhler, Hoppe-Seyler's Z. physiol. Chem., 242, 171 (1936).
  <sup>282</sup> Rothstein, Bull. soc. chim. France, [5] 2, 80 (1935).
  <sup>283</sup> Noyes and Cox, J. Am. Chem. Soc., 25, 1093 (1903).
  <sup>284</sup> Dey and Doraiswami, J. Ind. Chem. Soc., 10, 309 (1933).
  <sup>285</sup> Hoffmann, J. Org. Chem., 15, 425 (1950).
  <sup>286</sup> Eykman, Chem. Weekblad, 6, 699 (1909).
  <sup>287</sup> Buu-Hoi and Cagniant, Bull. soc. chim. France, [5] 9, 99 (1942).
  <sup>288</sup> Gagnon, Savard, Gaudry, and Richardson, Can. J. Research, 25B, 28 (1947).
  289 Birch and Robinson, J. Chem. Soc., 1942, 488.
  <sup>290</sup> Rajzman, Bull. soc. chim. France, 1948, 754.
  <sup>291</sup> Buu-Hoi, Cagniant, and Janicaud, Compt. rend., 212, 1105 (1941).

    Buu-Hoi, Cagniant, and Janicaud, Compr.
    Labs. Bellevue Paris, 1951, 292 [C. A.,

46, 416 (1952)].
  <sup>293</sup> Perkin and Prentice, J. Chem. Soc., 59, 990 (1891).
  <sup>294</sup> Tutin, J. Chem. Soc., 91, 1141 (1907).
  <sup>295</sup> Perkin and Scarborough, J. Chem. Soc., 119, 1400 (1921).
  <sup>296</sup> Dressel and Guthzeit, Ann., 256, 171 (1890).
  <sup>297</sup> Guthzeit and Dressel, Ber., 21, 2233 (1888).
  <sup>298</sup> Zelinsky, Ber., 22, 3294 (1889).
  <sup>299</sup> Perkin, J. Chem. Soc., 59, 798 (1891).
  300 Kötz and Stalmann, J. prakt. Chem., [2] 68, 156 (1903).
  301 Pospischill, Ber., 31, 1950 (1898).
  302 Thole and Thorpe, J. Chem. Soc., 99, 2183 (1911).
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similar reaction involving benzylidene chloride and tetraethyl 1,1,5,5pentanetetracarboxylate led to the formation of the doubly unsaturated

$$\mathrm{CH_2[CH(CO_2C_2H_5)_2]_2} + \mathrm{CH_2I_2} \xrightarrow{\mathrm{NaOC_2H_5}} \overset{\mathrm{(CO_2C_2H_5)_2}}{\overset{\mathrm{(CO_2C_2C_2H_5)_2}}{\overset{\mathrm{(CO_2C_2H_5)_2}}{\overset{\mathrm{(CO_2C_2H_5)_2}}{\overset{\mathrm{(CO_2C$$

acid  $\alpha, \alpha'$ -dibenzylidenepimelic acid, after saponification and decarboxylation,303 rather than a cyclic compound.

Chloroform, bromoform, iodoform, ethyl trichloroacetate, carbon tetrachloride, and carbon tetrabromide all react with diethyl sodiomalonate to form diethyl  $\alpha, \gamma$ -dicarbethoxyglutaconate, although a similar reaction with 1,1,1-trichloroethane failed. Analogous products are formed with

$$\text{CHCl}_3 + 2\text{CH}_2(\text{CO}_2\text{C}_2\text{H}_5)_2 \xrightarrow{\text{C}_2\text{H}_5\text{OH}} (\text{C}_2\text{H}_5\text{O}_2\text{C})_2\text{CHCH} = \text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$$

other active methylene compounds including ethyl cyanoacetate and malononitrile.<sup>231</sup> If monoalkylmalonic esters are utilized in a similar reaction, a mixture of products is formed in which either one or two of the halogen atoms of the haloform is retained.231

$$\begin{split} \text{CH}_3\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 + \text{CHCl}_3 &\xrightarrow{\text{Na.} (\text{C}_2\text{H}_5)_2\text{O}} \\ &+ (\text{C}_2\text{H}_5\text{O}_2\text{C})_2\text{C}(\text{CH}_3)\text{CHClC}(\text{CH}_3)(\text{CO}_2\text{C}_2\text{H}_5)_2 \end{split}$$

 $\alpha,\omega\text{-Polymethylene}$  dihalides have served as useful alkylating agents for the preparation of carbocyclic compounds with ring sizes ranging from three to seven. 92,170,269,304-310 A competing reaction results in the

$$\begin{array}{c} {\rm Br}({\rm CH}_2)_5 {\rm Br} \, + \, {\rm CH}_2({\rm CO}_2 {\rm C}_2 {\rm H}_5)_2 & \xrightarrow{{\rm NaOC}_2 {\rm H}_5, {\rm C}_2 {\rm H}_5 {\rm OH}} & \xrightarrow{{\rm CO}_2 {\rm C}_2 {\rm H}_5} \\ \\ & + \, ({\rm C}_2 {\rm H}_5 {\rm O}_2 {\rm C})_2 {\rm CH}({\rm CH}_2)_5 {\rm CH}({\rm CO}_2 {\rm C}_2 {\rm H}_5)_2 \end{array}$$

<sup>303</sup> Perkin and Prentice, J. Chem. Soc., 59, 818 (1891).

<sup>304</sup> Dox and Yoder, J. Am. Chem. Soc., 43, 1366 (1921). 303 Knowles and Cloke, J. Am. Chem. Soc., 54, 2028 (1932).

<sup>306</sup> Case, J. Am. Chem. Soc., 56, 715 (1934).

<sup>307</sup> Weston, J. Am. Chem. Soc., 68, 2345 (1946).

<sup>308</sup> Haworth and Perkin, J. Chem. Soc., 65, 86 (1894). 309 Carpenter and Perkin, J. Chem. Soc., 75, 921 (1899).

<sup>310</sup> Best and Thorpe, J. Chem. Soc., 95, 685 (1909).

simultaneous formation of the tetralkyl polymethylene- $\alpha,\omega$ -dimalonate.<sup>311</sup> Although this tetracarboxylic ester is usually formed by attack of two diethyl malonate anions on the dihalide,<sup>312</sup> the cyclopropane derivative obtained when ethylene dibromide serves as the alkylating agent has been found to be susceptible to attack by the enolate of an active methylene compound.<sup>310,312–314</sup> Thus the tetracarboxylic ester could be formed by either of two routes. The yield of the cyclopropane is better if ethyl cyanoacetate is substituted for diethyl malonate. As would be anticipated, the use of a large volume of solvent favors intramolecular alkylation leading to a cyclic product.<sup>210,307</sup>

A similar synthesis of cyclopropane derivatives utilizes 1,4-dibromo-2-butene as the alkylating agent. The major products are tetraethyl 2-vinyl-1,1,4,4-butanetetracarboxylate and diethyl 2-vinyl-1,1-cyclopropanedicarboxylate, the cyclopropane derivative apparently having been formed by an intramolecular  $S_N2'$  process (p. 112).

$$\begin{array}{c} {\rm BrCH_2CH = CHCH_2Br} + {\rm CH_2(CO_2C_2H_5)_2} \xrightarrow{NaOc_2H_5} \\ {\rm CH_2 = CH - CH - C(CO_2C_2H_5)_2} + {\rm CH_2 = CH - CHCH(CO_2C_2H_5)_2} \\ {\rm CH_2} & {\rm CH_2CH(CO_2C_2H_5)_2} \\ + ({\rm C_2H_5O_2C)_2CHCH_2CH = CHCH_2CH(CO_2C_2H_5)_2} \end{array}$$

It has proved difficult to arrest the reaction of polymethylene dihalides and sodiomalonic ester at the monoalkylation stage, since the intramolecular and intermolecular dialkylation reactions described previously

<sup>&</sup>lt;sup>311</sup> Freer and Perkin, J. Chem. Soc., 53, 215 (1888).

<sup>312</sup> Bone and Perkin, J. Chem. Soc., 67, 108 (1895).

<sup>313</sup> Mitchell and Therpe, J. Chem. Soc., 97, 997 (1910).

<sup>311</sup> Kierstead, Linstead, and Weedon, J. Chem. Soc., 1952, 3616.

often predominate. However, diethyl  $\gamma$ -bromopropylmalonate has been prepared in 70% yield by the use of a large excess of 1,3-dibromopropane with diethyl malonate. An alternative synthesis for such compounds involves the initial formation of a terminal methylene derivative of malonic ester followed by the peroxide-eatalyzed addition of hydrogen bromide. 210,315

Monoalkylation of diethyl sodiomalonate with 1-ehloro-3-iodopropane would be expected to produce diethyl  $\gamma$ -ehloropropylmalonate, displacement having involved the more reactive earbon-iodine bond. However, the alcohol-soluble sodium iodide produced in the reaction mixture converted the chloro ester in part to the corresponding iodo compound. When excess sodium iodide was added to the reaction mixture, only diethyl  $\gamma$ -iodopropylmalonate could be isolated. In the preparation of diethyl ( $\beta$ -chloroethyl)isoamylmalonate from 1-ehloro-2-iodoethane and diethyl isoamylmalonate this problem was avoided by the use of a benzene solution in which sodium iodide is insoluble.

Where one of the halogens of the dihalide is bonded to a secondary earbon atom, some dehydrohalogenation may be expected to accompany alkylation.<sup>160</sup> Halogen atoms bonded to tertiary earbon atoms are lost as the corresponding hydrogen halide.<sup>173,317,318</sup>

As described earlier (p. 125) certain vicinal dihalides, especially those compounds in which the halogen atoms are bonded to secondary and tertiary carbon atoms, tend to lose the halogen with the resulting formation of an olefin and the coupled product from two molecules of the active methylene compound. Other vicinal dihalides such as 1,2-dichlorocyclohexane, 120,120 tibromocyclohexane, 150,286,319 1,2-dibromotetrahydronaphthalene, 120,320 and 2,3-dibromodecahydronaphthalene

$$Cl + CH(CO_2C_2H_5)_2 - CH(CO_2C_2H_5)_2 + Cl^2$$

both alkylation and dehydrohalogenation reactions. Thus the product formed from the 1,2-dihalocyclohexanes was the same as the product formed from 2-cyclohexenyl ehloride or 2-cyclohexenyl bromide. 319 Since the alkylation of 1,2-dichlorocyclohexane with diethyl sodiomalonate proceeds much more rapidly than the analogous reaction with cyclohexyl chloride, 150 dehydrochlorination is presumed to be the first step in the sequence. With 2,3-dibromotetrahydronaphthalene reaction dehydrohalogenation occurred, the product being naphthalene.320

The reaction of 1,2-dithiocyanocyclohexane with diethyl malonate is completely analogous to the reaction of the 1,2-dihalocyclohexancs. One thiocyano group is lost in an elimination reaction, and the other group is displaced with the production of diethyl 2-cyclohexenylmalonate. 322

Vinyl and Aryl Halides. Although vinyl and aryl halides, being inert to nucleophilic displacement reactions, are generally of no value as alkylating agents, several successful alkylation reactions involving such halides have been reported. Thus 1,2-dibromoethylenc reacted with diethyl cthylmalonate to yield diethyl ethyl. (β-bromovinyl)malonate. 54 However, 1,2-dichloroethylene failed to alkylate malonic ester.<sup>275</sup> The successful alkylation of acetonitrile with chlorobenzenc in the presence of potassium amide and liquid ammonia<sup>323</sup> may be likened to the conversion of chlorobenzene to aniline under similar conditions,324 in which the amino group may become attached either to the carbon atom from which the chlorine atom is displaced or to an adjacent carbon atom. It is not known whether the position at which the cyanomethyl group enters and the position occupied by the leaving chlorine atom are the same.

If the carbon-halogen bond of the aryl halide is activated by the introduction of electron-attracting groups ortho and para to the halogen atom, then successful arylation will occur. For example, ethyl p-nitrophenylcyanoacetate has been prepared from p-nitrochlorobenzene and ethyl cyanoacetate. 325 However, it will be recalled that such electron-attracting substituents also promote decarbethoxylation (p. 127). When dicthyl 2,4-dinitrophenylmalonate was treated with 2,4-dinitrobromobenzene in 2,4-dinitrophenylmalonate was trouted bis-(2,4-dinitrophenyl)acetate cthanolic sodium etnoxide, omy carry (principal) acetate could be isolated. Replacement of halogen atoms situated on negatively substituted benzene rings by hydrogen has also been observed during alkylation reactions.326-328

<sup>321</sup> Cagniant and Buu-Hoi, Bull. soc. chim. France, [5] 9, 111 (1942).

<sup>322</sup> Mousseron and Winternitz, Bull. soc. chim. France, [5] 11, 120 (1044). 323 Bergstrom and Agostinho, J. Am. Chem. Soc., 67, 2152 (1945).

Bergstrom and Agostinho, J. Am. Oncin. 2021, 48. Chem. Soc., 75, 3290 (1953).

<sup>323</sup> Fairbourne and Fawson, J. Chem. Soc., 1927, 46.

<sup>326</sup> Jackson and Robinson, Am. Chem. J., 11, 93 (1889). 327 Jackson and Robinson, Am. Chem. J., 11, 541 (1889).

<sup>&</sup>lt;sup>228</sup> Jackson and Robinson, Ber., 21, 2034 (1888).

The 2- and 4-halopyridines and the 2- and 4-chloroquinolines, whose reactivity may be likened to that of the nitrochlorobenzenes just described, also serve as effective alkylating agents.

Epoxides. Epoxides have served as alkylating agents for malonic esters, cyanoacetic esters, monocarboxylic esters, and mononitriles. Except in sterically unfavorable instances, the intermediate hydroxy esters or hydroxy nitriles are converted to the corresponding lactones or cyclic imido esters. 27,329 The same products are formed if the corresponding alkene halohydrins are utilized.

Dialkyl Carbonates. The dialkyl carbonates cannot be used to alkylate malonic ester, 330 monocarboxylic esters, 43,129,331,332 or mononitriles 185,186,189,333 because carbethoxylation of the intermediate anion (p. 128) takes precedence over alkylation. With primary alkylmalonic esters the dialkyl carbonates may be used as alkylating agents, the dialkylated product being obtained in yields of 25–80%. The dialkyl carbonates are unsatisfactory alkylating agents for secondary alkylmalonic esters and for alkyleyanoacetic esters. 330

Dialkyl Sulfates, Alkyl Sulfonates, and Nitrates. Both dimethyl sulfate and diethyl sulfate have been used extensively for the alkylation of all types of active methylene compounds. The yields obtained with these alkylating agents and with the corresponding alkyl iodides are usually similar. In addition the high boiling points of the dialkyl sulfates permit the use of higher reaction temperatures without loss of the alkylating agent.<sup>249</sup>

The alkyl benzenesulfonates and the alkyl p-toluenesulfonates have been used to advantage as alkylating agents. As in the case of the alkyl halides the yields of alkylated products derived from primary alkyl sulfonates are good, but only fair yields are obtained with the sulfonate esters of secondary alcohols. In addition to their high boiling points, the alkyl sulfonates are valuable alkylating agents where conversion of the corresponding alcohol to the alkyl halide is difficult or involves rearrangement. 338, 334, 335

Benzyl nitrate has served as an alkylating agent for malonic ester, both mono- and di-alkylation products being obtained.  $^{336}$ 

<sup>&</sup>lt;sup>329</sup> Easton, Gardner, and Stevens, J. Am. Chem. Soc., 69, 2941 (1947).

Wallingford and Jones, J. Am. Chem. Soc., 64, 578 (1942).
 Nelson and Cretcher, J. Am. Chem. Soc., 50, 2758 (1928).

<sup>332</sup> Hauser, Abramovitch, and Adams, J. Am. Chem. Soc., 64, 2714 (1942).

<sup>333</sup> Hessler, Am. Chem. J., 32, 119 (1904).

<sup>334</sup> Braker, Pribyl, and Lott, J. Am. Chem. Soc., 69, 866 (1947).

<sup>Peacock and Tha, J. Chem. Soc., 1928, 2303.
Nef, Ann., 309, 171 (1899).</sup> 

component in an acetic acid-piperidine mixture is hydrogenated over palladium on charcoal. This process, termed reductive alkylation, has been found to produce certain alkylevanoacetic esters in yields of 39-98%.362-364

Reductions of alkylidene derivatives and reductive alkylation are advantageous in that dialkylation, a side reaction in alkylation procedures, is avoided.363 The use of platinum oxide as the entalyst for reductive alkylation may result in partial reduction of the nitrile group in addition to the expected reductive alkylation.363

Addition of Grignard Reagents to Alkylidene Derivatives (Tables XVIII and XIX). Extensive dehydrohalogenation precludes the use of tertiary alkyl halides for the preparation of tertiary alkyl derivatives of active methylene compounds (pp. 112, 124, 139). Such tertiary alkyl derivatives can be prepared by the addition of Grignard reagents to the alkylidene derivatives obtained by the condensation of malonic or eyanoacetic esters with a ketone. The mode of addition of Grignard reagents to

$$(\mathrm{CH_3})_2\mathrm{C} = \mathrm{C}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2 + \mathrm{CH}_3\mathrm{MgI} \rightarrow (\mathrm{CH_3})_3\mathrm{CCH}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$$
 
$$\longrightarrow \mathrm{C}(\mathrm{CN})\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5 + \mathrm{C}_6\mathrm{H}_5\mathrm{MgBr} \rightarrow \bigcirc_{\mathrm{C}_6\mathrm{H}_5}\mathrm{CH}(\mathrm{CN})\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5$$

substituted cinnamonitriles is dependent on the structure of the unsaturated compound. Normally, 1,2 addition occurs forming an imino compound; 365,366 however, if a large group is bonded to the α-earbon atom, 1,4 addition leading to a saturated nitrile has been observed. 365,366 The addition of aliphatic Grignard reagents to alkylidene derivatives is often accompanied by reduction of the double bond in the alkylidene compound as a side reaction.367 The substitution of the appropriate dialkyl- or diarylcadmium for the Grignard reagent has resulted in the formation of the alkylated product in poor yield.367 The addition of copper salts to the reaction mixture has been reported to favor the 1,4-addition of Grignard reagents to alkylidenemalonic esters.368

Condensation of Aromatic Compounds with Mesoxalic and Tartronic Esters (Table XX). Direct alkylation methods usually cannot be applied to the preparation of aryl- and diaryl-malonic esters (p. 143).

and the same of

<sup>&</sup>lt;sup>363</sup> Alexander and Cope, J. Am. Chem. Soc., 66, 886 (1944).

<sup>364</sup> Sharp and Dohme, Brit. pat. 606,962 [C. A., 43, 1436 (1949)]. 365 Kohler, Am. Chem. J., 35, 386 (1906).

<sup>366</sup> Henze and Swett, J. Am. Chem. Soc., 73, 4918 (1951).

<sup>367</sup> Prout, Huang, Hartman, and Korpies, J. Am. Chem. Soc., 76, 1911 (1954). 368 Brandström and Forsblad, Arkiv Kemi, 6, 561 (1954).

Aryl-substituted malonic esters have been obtained from diethyl mesoxalate, an oxidation product of diethyl malonate. 369 The aryltartronic esters have been obtained either by the condensation of mesoxalic ester with aromatic hydrocarbons in the presence of sulfuric acid or stannic chloride<sup>370,371</sup> or by the addition of Grignard reagents to mesoxalic ester

$$\mathrm{OC(CO_2C_2H_5)_2} + \underbrace{\begin{array}{c} \mathrm{CH_3} \\ \mathrm{SnCl_4} \end{array}}_{\mathrm{CH_3}} \underbrace{\begin{array}{c} \mathrm{CH_3} \\ \mathrm{I} \\ \mathrm{CC(CO_2C_2H_5)_2} \end{array}}_{\mathrm{CH_3}}$$

at -70%.372 Diethyl 9-phenanthryltartronate has been converted to 9-phenanthrylmalonic ester by the replacement of the hydroxyl group by a chlorine atom followed by reduction.372

The diarylmalonic esters have been prepared by the condensation of aromatic hydrocarbons with either mesoxalic esters or aryltartronic esters in the presence of sulfuric acid or phosphorus oxychloride.373

$$\begin{array}{c} \text{OH} \\ p\text{-(CH}_3)_2\text{NC}_6\text{H}_4\text{C(CO}_2\text{C}_2\text{H}_5)_2 + (\text{CH}_3)_2\text{NC}_6\text{H}_5 \xrightarrow{\text{POCl}_3} \end{array}$$

$$[p\text{-}(\text{CH}_3)_2\text{NC}_6\text{H}_4]_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$$

Other Methods. Among other methods available for the preparation of alkyl- or aryl-malonic esters is the condensation of diethyl oxalate with the appropriately substituted acetic ester. 179 The resultant ethoxalvl derivative is then decarbonylated thermally with 374 or without 375-378 powdered soft glass. This method is of value not only for the preparation

$$\begin{split} \mathbf{C_6H_5CH_2CO_2C_2H_5} + &(\mathbf{CO_2C_2H_5})_2 \xrightarrow{\mathbf{NaoC_2H_5}} &\mathbf{C_6H_5CH(CO_2C_2H_5)COCO_2C_2H_5} \\ &\mathbf{C_6H_5CH(CO_2C_2H_5)COCO_2C_2H_5} \rightarrow &\mathbf{CO} \, + \, \mathbf{C_6H_5CH(CO_2C_2H_5)_2} \end{split}$$

<sup>&</sup>lt;sup>369</sup> Dox, Org. Syntheses, Coll. Vol. 1, John Wiley & Sons, New York, 1941, p. 266.

<sup>370</sup> Riebsomer and Irvine, Org. Syntheses, 25, 33 (1945).

<sup>371</sup> Riebsomer, Wiseman, and Condike, Proc. Indiana Acad. Sci., 50, 80 (1940) [C. A., 35.

<sup>372</sup> Copc and Field, J. Org. Chem., 14, 856 (1949).

<sup>373</sup> Guyot and Michel, Compt. rend., 148, 229 (1909).

<sup>374</sup> Blicke and Zienty, J. Am. Chem. Soc., 63, 2779 (1941).

<sup>375</sup> Rising and Stieglitz, J. Am. Chem. Soc., 40, 723 (1918).

<sup>376</sup> Kcach, J. Am. Chem. Soc., 55, 3440 (1933).

<sup>377</sup> Lauer and Hansen, J. Am. Chem. Soc., 61, 3039 (1939).

Lauer and Hansen, J. Am. Chem. Soc., 65, 121
 Levene and Meyer, Org. Syntheses, Coll. Vol. 2, John Wiley & Sons, New York, 1943, p. 288.

of arylmalonic esters unobtainable by direct alkylation,<sup>379</sup> but also for the preparation of low-molecular-weight monoalkylmalonic esters whose separation from the malonic ester and dialkylmalonic ester present in the product obtained by direct alkylation is difficult (p. 123).<sup>69,380,381</sup>

A more direct method of carbethoxylation involves the use of diethyl carbonate in the presence of sodium ethoxide. This method is applicable to the synthesis of alkyl and aryl derivatives of malonic ester<sup>43</sup>, <sup>129</sup>, <sup>330-332</sup> and cyanoacetic ester, <sup>185-189</sup>, <sup>331</sup>, <sup>333</sup> the best yields being obtained in the case of the aryl derivatives. Dialkylacetic esters cannot be carbethoxylated by this method. <sup>43</sup>

The alkylation of aromatic hydrocarbons with α-bromoarylacetic esters, α-bromoarylacetonitriles, or α-bromodiarylacetonitriles in a Friedel-Crafts reaction has served to produce diarylacetic esters, diarylacetonitriles, 27,382,383 and triarylacetonitriles. 383

Diethyl cyclopropylmalonate has been prepared from cyclopropanecarboxylic acid by means of the reaction sequence illustrated with the accompanying equations.<sup>384</sup>

The alkylation of eyanoketene dimethyl acetal with benzyl bromide gave, after acidification, methyl benzyleyanoacetate (21%) and methyl dibenzyleyanoacetate (26%).385

#### SYNTHETIC APPLICATIONS OF THE ALKYLATION REACTION

The alkylation of active methylene compounds affords a convenient synthetic route to mono-, di-, and tri-substituted derivatives of acetic acid and acetonitrile in which the carbon chain of the alkylating agent has been lengthened by two atoms. Substituted acetic acids are often prepared from the corresponding malonic esters by saponification with aqueous alkali (p. 157) followed by decarboxylation of the substituted malonic acid. With ethyl esters the course of the saponification step may be followed by distilling the ethanol from the reaction mixture as it is formed. With low-molecular-weight substituted malonic acids, decarboxylation is most easily effected by boiling a solution of the malonic acid in 20% (constant-boiling) aqueous hydrochloric acid or aqueous sulfuric acid. The saponification and decarboxylation may be done in the same reaction vessel if a calculated excess of concentrated hydrochloric or sulfuric acid is added to the reaction mixture obtained from the saponification.14,386 It is usually more satisfactory to isolate substituted malonic acids of high molecular weight. These acids lose carbon dioxide when they are heated above their melting points.387 Alternatively, a solution of the substituted malonic acid in a high-boiling solvent such as xylene may be boiled under reflux until decarboxylation is complete.

$$\underset{R''}{\overset{R}{\nearrow}} C(CO_2C_2H_5)_2 \xrightarrow[R']{\overset{R}{\rightarrow}} C(CO_2{}^{\circledcirc}N_8{}^{\circledcirc})_2 \xrightarrow[R']{\overset{R}{\rightarrow}} C(CO_2H)_2 \xrightarrow[R']{\overset{R}{\rightarrow}} CHCO_2H + CO_2$$

The saponification of substituted cyanoacetic esters followed by the thermal decarboxylation of the corresponding cyanoacetic acid yields substituted acetonitriles.

$$\overset{R}{\underset{R'}{\nearrow}}C(CN)CO_2C_2H_5 \overset{R}{\underset{R'}{\rightarrow}}C(CN)CO_2{}^{\ominus}Na{}^{\ominus} \overset{R}{\underset{R'}{\rightarrow}}C(CN)CO_2H \overset{R}{\underset{R'}{\rightarrow}}CHCN + CO_2$$

Substituted malonic and cyanoacetic esters may be hydrolyzed and decarboxylated to yield substituted acetic acids in one step by treatment with boiling aqueous acids.<sup>388</sup>

<sup>388</sup> Reid and Ruhoff, Org. Syntheses, Coll. Vol. 2, John Wiley & Sons, New York, 1943, p. 474.

<sup>387</sup> Marvel and du Vigneaud, Org. Syntheses, Coll. Vol. 2, John Wiley & Sons, New York, 1943, p. 94.

<sup>&</sup>lt;sup>388</sup> Clarke and Murray, Org. Syntheses, Coll. Vol. 1, John Wiley & Sons, New York, 1941, p. 523.

 $t ext{-Butyl}, ^{389}$  tetrahydropyranyl,  $^{390}$  and benzhydryl $^{224}$  esters of substituted malonic acids undergo fission of the carbon-oxygen bond of the ester in acidic media. This rapid fission of t-butyl esters  $^{392}$  and tetrahydropyranyl esters390 has been utilized for the synthesis of easily reducible ketones, 390,393

$$\begin{split} p \cdot \mathrm{O_2NC_6H_4COC(CH_2C_6H_5)(CO_2C_4H_9 \cdot t)_2} \xrightarrow{\mathrm{H}^{\textcircled{\tiny{\textcircled{\tiny{0}}}}}} p \cdot \mathrm{O_2NC_6H_4COCH_2CH_2C_6H_5} \\ &+ 2\mathrm{CO_2} + 2\mathrm{(CH_3)_2C} = \mathrm{CH_2} \end{split}$$

by the acidic hydrolysis and decarboxylation of acylmalonic esters. The use of benzyl esters394-396 which can be cleaved by hydrogenolysis397 is not feasible for the synthesis of compounds with easily reducible groups. The use of the acid-labile t-butyl and tetrahydropyranyl esters is to be recommended for the preparation of substituted malonic or cyanoacetic acids containing other functions which would not survive the reaction conditions required for the hydrolysis of the ethyl esters. The reversible nature of the acidic cleavage permits the synthesis of t-butyl esters by the condensation of carboxylic acids and isobutylene in an acidic medium;393 tetrahydropyranyl esters may be prepared similarly from dihydropyran.

$${\rm CH_2(CO_2H)_2}\,+\,2({\rm CH_3)_2C}\,{=}\,{\rm CH_2}\,+\,2{\rm H}^{\,\oplus} \rightleftharpoons {\rm CH_2(CO_2C_4H_9}{\cdot}t)_2$$

An alternative method for the conversion of diethyl dialkylmalonates to ethyl dialkylacetates involves the removal of a carbethoxyl group at high temperatures. This change is most easily effected by heating an ethanolic solution of the diethyl dialkylmalonate to 250° in the presence of sodium ethoxide (p. 127). Under such conditions diethyl diethylmalonate was converted to ethyl diethylacetate in 82% yield. When an ethereal solution of diethyl diethylmalonate was heated with 2 gram atoms of sodium metal, carbon monoxide (85%) was evolved and ethyl

<sup>388</sup> Cohen and Schneider, J. Am. Chem. Soc., 63, 3382 (1941).

<sup>390</sup> Bowman and Fordham, J. Chem. Soc., 1952, 3945.

<sup>391</sup> Strain, Plati, and Warren, J. Am. Chem. Soc., 64, 1436 (1942).

<sup>392</sup> Breslow, Baumgarten, and Hauser, J. Am. Chem. Soc., 66, 1286 (1944).

<sup>393</sup> Fonken and Johnson, J. Am. Chem. Soc., 74, 831 (1952).

<sup>394</sup> Bowman, J. Chem. Soc., 1950, 325.

<sup>395</sup> Ames and Bowman, J. Chem. Soc., 1951, 1079.

<sup>396</sup> Bowman and Fordham, J. Chem. Soc., 1951, 2758.

<sup>397</sup> Hartung and Simonoff in Adams, Organic Reactions, Vol. 7, Chapter 5, John Wiley & Sons, New York, 1953, pp. 263-326.

diethylacetate was formed in 46% yield.<sup>398</sup> Similarly, diethyl diethylmalonate, when heated with ethanol-free sodium ethoxide to 220–230°, yielded ethyl diethylacetate (67%), ether (8%), diethyl carbonate (16%), ethylene (14%), carbon monoxide (25%), and ethanol.<sup>180</sup> The diethyl carbonate was presumably formed from the ethanol generated in the reaction mixture (p. 127).

Substituted acetic acids prepared by means of the alkylation reaction have been used to prepare long-chain hydrocarbons of known structure, 46,141,399,400 hydrindones, 114,401–410 tetralones, 321,411–423 and hydrotetralones, 424–426

A number of amino acid syntheses have utilized such starting materials as chloromalonic ester, <sup>209</sup> alkylmalonic esters, <sup>118,119,132,427–433</sup> aminomalonic

```
398 Krollpfoiffer and Rosenberg, Ber., 69, 465 (1936).
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- 399 Levene and Taylor, J. Biol. Chem., 54, 351 (1922).
- 400 Grimshaw, Guy, and Smith, J. Chem. Soc., 1940, 68.
- <sup>401</sup> Lecocq, Ann. chim. Paris, [12] 3, 62 (1948).
- <sup>402</sup> von Braun and Friedsam, Ber., 65, 1680 (1932).
- 403 Cagniant and Buu-Hoi, Bull. soc. chim. France, [5] 9, 119 (1942).
- 404 Cagniant, Bull. soc. chim. France, [5] 9, 884 (1942).
- 405 Buu-Hoi and Cagniant, Bull. soc. chim. France, [5] 10, 151 (1943).
- <sup>408</sup> Fieser and Seligman, J. Am. Chem. Soc., 57, 2174 (1935).
- <sup>407</sup> Bruce and Kahn, J. Am. Chem. Soc., 60, 1017 (1938).
- 408 Bruce and Todd, J. Am. Chem. Soc., 61, 157 (1939).
- 409 Fieser and Gates, J. Am. Chem. Soc., 62, 2335 (1940).
- 410 Martin, J. Chem. Soc., 1941, 679.
- 411 Lévy, Ann. chim. Paris, [11] 9, 44 (1938).
- 412 Buchta, Galster, and Luther, Chem. Ber., 82, 126 (1949).
- 413 Cagniant and Buu-Hoï, Bull. soc. chim. France, [5] 9, 841 (1942).
- 414 Buu-Hoi and Cagniant, Compt. rend., 214, 115 (1942).
- 415 Ruzicka and Mingazzini, Helv. Chim. Acta, 5, 710 (1922).
- 416 Ruzicka and Ehmann, Helv. Chim. Acta, 15, 140 (1932).
- 417 Ruzicka, Ehmann, and Mörgeli, Helv. Chim. Acta, 16, 314 (1933).
- 418 Rapson and Short, J. Chem. Soc., 1933, 128.
- 419 Kon, Narracott, and Reid, J. Chem. Soc., 1938, 778.
- 420 Cocker and Hayes, J. Chem. Soc., 1951, 844.
- 421 Chakravarti, J. Indian Chem. Soc., 20, 393 (1943).
- 422 Dhekne and Bhide, J. Indian Chem. Soc., 28, 504 (1951).
- 423 Späth and Hromatka, Monatsh. Chem., 60, 117 (1932).
- <sup>424</sup> Chuang, Tien, and Ma, Ber., 69, 1494 (1936).
- <sup>425</sup> Cook and Lawrence, J. Chem. Soc., 1935, 1637.
- 425 Cook and Lawrence, J. Chem. Soc., 1937, 817.
- <sup>427</sup> Fischer and Schmitz, Ber., 39, 351 (1906).
- 428 Fischer and Schmitz, Ber., 39, 2209 (1906).
- 429 von Braun and Kruber, Ber., 45, 384 (1912).
- 430 Curtius and Sieber, Ber., 55, 1543 (1922).
- 431 Sayles and Degering, J. Am. Chem. Soc., 71, 3161 (1949).
- 432 Carter, J. Biol. Chem., 108, 619 (1935).
- 433 Barry and Hartung, J. Org. Chem., 12, 460 (1947).

acetamidomalonic ester,246, 436, 437 formamidomalonic ester, 233, 453, 458, 459 esters.434, 435 benzamidomalonic ester. 49,232,234,235,438-452,454-457 phthalimidomalonic ester, 236, 160-468 alkylcyanoacetic esters, 469-472 and acylaminocyanoacctic esters. 241,242,448

The reaction sequence utilized for the preparation of amino acids from aminomalonic esters, acylaminomalonic esters, or acylaminocyanoacetic esters involves alkylation followed by saponification and decarboxylation. Finally the acyl group is removed by acid hydrolysis. By the appropriate

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\text{RCONHCH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \rightarrow \text{RCONHC}(\text{R}')(\text{CO}_2\text{C}_2\text{H}_5)_2
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 $\rightarrow \text{RCONHCH(R')CO}_2\text{H} \rightarrow \text{R'CH(NH}_2)\text{CO}_2\text{H}$ 

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434 Putochin, Ber., 56, 2213 (1923).
 435 Locquin and Cerchez, Bull. soc. chim. France, [4] 47, 1386 (1930).
 436 Capková-Jirků, Koštíř, and Vondráček, Chem. Listy, 44, 19 (1950) [C. A., 45, 8004
(1951)].
  437 Weisiger, J. Biol. Chem., 186, 591 (1950).
  438 Harington, Biochem. J., 43, 434 (1948).
  439 Sorm and Prochazka, Chem. Listy, 46, 490 (1952) [C. A., 47, 3798 (1953)].
  140 Erlenmeyer and Grubenmann, Helv. Chim. Acta, 30, 297 (1947).
  441 Snyder and Pilgrim, J. Am. Chem. Soc., 70, 1962 (1948).
   412 Goering, Cristol, and Dittmer, J. Am. Chem. Soc., 70, 3310 (1948).
   463 Jones and McLaughlin, J. Am. Chem. Soc., 71, 2444 (1949).
   444 Bennett and Niemann, J. Am. Chem. Soc., 72, 1800 (1950).
   463 Bennett and Niemann, J. Am. Chem. Soc., 72, 1806 (1950).
   466 Jones, Kornfeld, and McLaughlin, J. Am. Chem. Soc., 72, 4526 (1950).
   447 Degering and Boatright, J. Am. Chem. Soc., 72, 5137 (1950).
    449 Burckhalter and Stephens, J. Am. Chem. Soc., 73, 56 (1951).
    44 Albertson, J. Am. Chem. Soc., 73, 452 (1951).
    450 Caldwell and Fox, J. Am. Chem. Soc., 73, 2935 (1951).
    451 Burckhalter and Stephens J. Am. Chem. Soc. 73, 3502 (1951).
    451 Herz, Dittmer, and Cristol, J. Biol. Chem., 171, 383 (1947).
    453 Evans and Walker, J. Chem. Soc., 1947, 1571.
    454 Elliott and Harington, J. Chem. Soc., 1949, 1374.
    455 Marnalis, Petrow, and Sturgeon, J. Chem. Soc., 1950, 1600.
     434 Dalglirds, J. Chem. Soc., 1952, 137.
     437 Arnistrong and Lewis, J. Org. Chem., 17, 618 (1952).
     414 Niemann, Lewis, and Hays, J. Am. Chem. Soc., 64, 1678 (1942).
     139 Dunn, Smart, Redemann, and Brown, J. Biol. Chem., 94, 599 (1931-1932).
     445 Kuhn and Quadbeck, Ber., 76, 527 (1943).
     441 Kuhn and Quadbeck, Ber., 76, 529 (1943).
      442 Sorensen, Bull. soc. chim. France, [3] 33, 1042 (1905).
      443 Sorensen, Bull. soc. chim. France, [3] 33, 1052 (1905).
      444 Dey. J. Chem. Soc., 1937, 1166.
      463 Booth, Burnop, and Jones, J. Chem. Soc., 1944, 666.
      444 Barger and Weichselbaum, Org. Syntheses, Coll. 1'ol. 2, John Wiley & Sons, New York,
    1943, p. 384.
       111 Dunn and Smart, Org. Syntheses, 30, 7 (1950).
       444 Overhoff, Boeke, and Gorter, Rec. trav. chim., 55, 293 (1930).
```

449 Gagnon and Nolin, Can. J. Research, 27B, 742 (1949). Carnon, Boivin, and Craig, Can. J. Chemistry, 29, 70 (1951).

472 Cartius and Benekiser, J. prakt. Chem., [2] 125, 236 (1930).

111 Boivin, Gagnon, Renaud, and Bridgeo, Can. J. Chemistry, 30, 994 (1952).

$$\rm RCH(CO_2K)CO_2C_2H_5 \xrightarrow{-N_2H_4} RCH(CO_2K)CONHNH_2 \xrightarrow{-HNO_2}$$

$$\begin{array}{c|c} \text{CO-O} & \\ \text{RCH(CO}_2\text{K)CON}_3 \rightarrow \text{RCH} & \rightarrow \text{RCH(NH}_2\text{)CO}_2\text{H} \\ \text{NH-CO} & \end{array}$$

$$\begin{split} \text{RCH(CN)CO}_2\text{C}_2\text{H}_5 &\xrightarrow{\text{N}_2\text{H}_4} \\ &\rightarrow \text{RCH(NH}_2)\text{CN} &\rightarrow \text{RCH(NH}_2)\text{CO}_2\text{H} \end{split}$$

and some large-ring compounds 219,269,306,492,493 are readily accessible with the use of dihalogenated alkylating agents or  $\omega$ -haloalkyl derivatives of active methylene compounds. Alkylating agents of the type  $Z(CH_2CH_2Cl)_2$ , where Z is an oxygen, sulfur, or nitrogen atom, have been used to synthesize tetrahydropyrans, 77,494,496–499 tetrahydrothiopyrans, 77,499 and piperidines. 77,495,501,503–505 The synthesis of certain polynuclear hydrocarbons by the method of Darzens 506–516 and by related

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<sup>492</sup> Kenner, J. Chem. Soc., 103, 613 (1913).
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<sup>493</sup> Franke and Hankam, Monatsh. Chem., 31, 177 (1910).

<sup>494</sup> von Braun and Köhler, Ber., 50, 1657 (1917).

<sup>495</sup> Büchi, Leuenberger, and Lieberherr, Farm. sci. e tec. Pavia, 6, 429 (1951) [C. A., 46, 8015 (1952).

<sup>496</sup> Kamm and Waldo, J. Am. Chem. Soc. 43, 2223 (1921).

<sup>497</sup> Henze and McKee, J. Am. Chem. Soc., 64, 1672 (1942).

<sup>498</sup> Gibson and Johnson, J. Chem. Soc., 1930, 2525.

<sup>499</sup> Eisleb, U.S. pat. 2,242,575 [C. A., 35, 5647 (1941)].

<sup>500</sup> Bergel, Morrison, and Rinderknecht J. Chem. Soc., 1944, 267.

<sup>501</sup> Morrison and Rinderknecht J. Chem. Soc. 1950, 1467.

<sup>502</sup> Avison and Morrison J. Chem. Soc., 1950, 1471.

<sup>503</sup> Eisleb, Brit. pat. 501,135 [C. A., 33, 5872 (1939)].

<sup>504</sup> Tanabe Drug Co., Jap. pat. 153,615 [C. A., 43, 3471 (1949)].

<sup>505</sup> Eisleb, U.S. pat. 2,167,351 [C. A., 33, 8923 (1939)].

<sup>506</sup> Darzens, Compt. rend., 183, 748 (1926).

<sup>507</sup> Darzens and Heinz, Compt. rend., 184, 33 (1927).

<sup>508</sup> Darzens, Compt. rend., 190, 1562 (1930).

<sup>500</sup> Darzens and Lévy, Compt. rend., 194, 2056 (1932).

<sup>510</sup> Darzens and Lévy, Compt. rend., 199, 1426 (1934).

Darzens and Lévy, Compt. rend., 200, 469 (1935).
 Darzens and Lévy, Compt. rend., 200, 2187 (1935).

<sup>213</sup> Darzens and Lévy, Compt. rend., 201, 730 (1935).

<sup>514</sup> Darzens and Levy, Compt. rend., 202, 427 (1936).

<sup>515</sup> Darzens and Lévy, Compt. rend., 203, 669 (1936).

<sup>516</sup> Campbell and Wang, J. Chem. Soc., 1949, 2186.

methods  $^{517-520}$  requires as intermediates suitably substituted allylmalonic esters.

$$\begin{array}{c} \text{CO}_2\text{H} \\ \\ \text{CH}_3 \\ \\ \text{S} \end{array} \xrightarrow{\text{CH}_3\text{CO}_2\text{H}}$$

Lactones are readily prepared by the treatment of epoxides with the metal enolates of malonic esters,  $^{8,11,12,282,521-527}$  cyanoacetic esters,  $^{528}$  or ethyl isobutyrate. Similarly, mononitriles are converted to cyclic imido esters,  $^{27,329}$  which may be hydrolyzed to lactones. The reaction of  $\alpha$ -bromoisobutyraldehyde with diethyl malonate produced an unsaturated lactone rather than a normal alkylation product.  $^{529}$ 

- 521 Traube and Lehmann, Ber., 32, 720 (1899).
- 522 Traube and Lehmann, Ber., 34, 1971 (1901).
- 523 Rothstein, Bull. soc. chim. France, [5] 2, 1936 (1935).
- 524 Rothstein and Fieini, Compt. rend., 234, 1293 (1952).
- 325 Rothstein and Ficini, Compt. rend., 234, 1694 (1952).
- 526 Russell and VanderWerf, J. Am. Chem. Soc., 69, 11 (1947).
- 227 Cavallito, Fruehauf, and Bailey, J. Am. Chem. Soc., 70, 3724 (1948).
- <sup>128</sup> Glickman and Cope, J. Am. Chem. Soc., 67, 1012 (1945).
- 529 Franke and Groeger, Monatsh. Chem., 43, 55 (1922).

<sup>&</sup>lt;sup>517</sup> Tatevosyan and Vardanyan, Zhur. Obshchei Khim. (J. Gen. Chem. U.S.S.R.), 19, 327 (1949) [C. A., 43, 6609 (1949)].

<sup>&</sup>lt;sup>518</sup> Tatevosyan and Vardanyan, Zhur. Obshchei Khim. (J. Gen. Chem. U.S.S.R.), 19, 332 (1949) [C. A., 43, 6609 (1949)].

<sup>&</sup>lt;sup>519</sup> Tatevosyan and Vardanyan, Zhur. Obshchei Khim. (J. Gen. Chem. U.S.S.R.), 21, 1170 (1951) [C. A., 46, 2036 (1952)].

<sup>&</sup>lt;sup>520</sup> Tatevosyan and Vardanyan, Zhur. Obsheheï Khim. (J. Gen. Chem. U.S.S.R.), 21, 1238 (1951) [C. A., 46, 2037 (1952)].

In the synthesis of barbituric acids, malonic esters, 15.35,125,126,129,144,203,278, cyanoacetic esters, 562,563 and malononitriles211 have found extensive use. The barbituric acids are formed when one of the aforementioned active methylene compounds is treated with urea or guanidine 563 in the presence of a base. The thiobarbituric acids35,126,552-555 have been prepared from thiourea in an analogous manner. The intermediate imino com-

$$\begin{array}{c} \text{CO-NH} \\ \text{R}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2 + \text{NH}_2\text{CONH}_2 \xrightarrow{\text{NaOC}_2\text{H}_5} & \begin{array}{c} \text{CO-NH} \\ \mid & \mid \\ \text{R}_2\text{C} & \text{CO} + 2\text{C}_2\text{H}_5\text{OH} \\ \mid & \mid \\ \text{CO-NH} \end{array} \end{array}$$

530 Reichert and Wilke, Arch. Pharm., 276, 596 (1938).

pounds formed in the reaction of substituted cyanoacetic esters or substituted malononitriles with urea or a urea derivative have been hydrolyzed with aqueous acid.

```
<sup>551</sup> Tanaka, Miyanaga, and Okami, Bull. Hyg. Research Inst. Japan, 35, 105 (1929) [C. A.,
24, 1086 (1930)].
  532 Tiffeneau, Bull. soc. chim. France, [4] 33, 183, (1923).
  233 Wichterle and Nemeček, Chem. Listy, 37, 105 (1943) [C. A., 44, 5815 (1950)].
  131 Morsman, Helv. Chim. Acta, 18, 1254 (1935).
  535 Renard and Dony, Ind. chim. belge, 16, 479 (1951) [C. A., 46, 10108 (1952)].
   536 Shonle and Moment, J. Am. Chem. Soc., 45, 243 (1923).
   537 Dox and Yoder, J. Am. Chem. Soc., 45, 1757 (1923).
   535 Dox. J. Am. Chem. Soc., 46, 1707 (1924).
   529 Dox. J. Am. Chem. Soc., 46, 2843 (1924).
   510 Volwiler, J. Am. Chem. Soc., 47, 2236 (1925).
   set Creteher, Koeh, and Pittenger, J. Am. Chem. Soc., 47, 3083 (1925).
    542 Hill and Keach, J. Am. Chem. Soc., 48, 257 (1926).
    543 Dox and Jones, J. Am. Chem. Soc., 50, 2033 (1928).
    544 Kirner and Richter, J. Am. Chem. Soc., 51, 3131 (1929).
    545 Volwiler and Tabern, J. Am. Chem. Soc., 52, 1676 (1930).
    146 Keach, J. Am. Chem. Soc., 55, 2975 (1933).
    547 Shonle and Waldo, J. Am. Chem. Soc., 55, 4649 (1933).
    548 Hooper and Johnson, J. Am. Chem. Soc., 56, 484 (1934).
     549 Kleiderer and Shonle, J. Am. Chem. Soc., 56, 1772 (1934).
     550 Shonle, Waldo, Keltch, and Coles. J. Am. Chem. Soc., 58, 585 (1936).
     551 Shonle and Doran, J. Am. Chem. Soc., 58, 1358 (1936).
     153 Doran and Shonle, J. Am. Chem. Soc., 59, 1625 (1937).
     353 Walter, Goodson, and Fosbinder, J. Am. Chem. Soc., 67, 659 (1945).
     334 Walter, Goodson, and Fosbinder, J. Am. Chem. Soc., 67, 661 (1945).
     523 Skinner and Mitchell, J. Am. Chem. Soc., 67, 1252 (1945).
     334 van Tamelen and Van Zyl, J. Am. Chem. Soc., 72, 2979 (1950).
```

<sup>237</sup> Walton, Doczi, and King, J. Am. Chem. Soc., 72, 4319 (1950). 234 Skinner and Huber, J. Am. Chem. Soc., 73, 3321 (1951).

141 Cope and Hancock, J. Am. Chem. Soc., 61, 776 (1939).

Oharn, Tamura, Ohmori, and Mochizuki, J. Pharm. Soc. Japan, 71, 911 (1951) [C. A., 111 Tatevosyan and Tuteryan, Zhur. Priklad. Khim. (J. Applied Chem. U.S.S.R.), 20,

430 Maynert, J. Biol. Chem., 195, 403 (1952).

287 (1947) [C. A., 43, 1725 (1949). 342 Conrad, Ann., 340, 310 (1905).

#### EXPERIMENTAL CONDITIONS AND PROCEDURES

If optimum yields are to be obtained from an alkylation reaction the apparatus, solvent, and reactants must be anhydrous. Although the maintenance of an inert (nitrogen) atmosphere in the reaction is advisable, this precaution is of prime importance if a high-boiling solvent is used or if the reaction is run at a temperature below the boiling point of the solvent. Without protection from the atmosphere afforded by solvent vapor or by an inert gas, many of the alkoxides and enolates are rapidly attacked by molecular oxygen.

If the alkylating agent is relatively volatile an excess of the reagent must be employed if the reaction is to go to completion. In such instances a desirable alternative is the use of dimethyl sulfate, diethyl sulfate, or the appropriate alkyl sulfonate. Although the completion of an alkylation can sometimes be determined by allowing the reaction to proceed until the reaction mixture becomes neutral, in many reactions complete neutrality is never reached. To determine the extent of alkylation in such cases it is advisable to remove aliquots of the reaction mixture periodically and to titrate them with a standard acid. To simplify subsequent extraction procedures the majority of the alcohol should be distilled from an alkylation reaction mixture before the mixture is poured into water.

Monoalkylmalonic esters must be boiled with 50% aqueous potassium hydroxide for two hours to effect saponification, 82,571 and dialkylmalonic esters require ten hours under similar conditions. 82,571 With less concentrated alkali longer reaction periods are required. The cyanoacetic esters are more rapidly hydrolyzed, the ester group of ethyl methyl-cyanoacetate being saponified almost instantly with 10% aqueous sodium hydroxide. 568 Similarly, ethyl dimethylcyanoacetate is saponified within twenty minutes. 568

The ease with which alkylidenecyanoacetic esters form water-soluble sodium bisulfite adducts permits these esters to be separated from their alkylation products, which do not react with sodium bisulfite. 37,64,214,344 Unchanged alkylidenemalonic esters also may be removed by treatment with aqueous ammonium hydroxide. Under such conditions the alkylidenc derivative is converted to the aldehyde or ketone and malonic ester in a reverse aldol reaction. The malonic ester so formed is converted to malonamide. 63

Diethyl n-Butylmalonate.<sup>13</sup> This Organic Syntheses procedure illustrates the standard method used for the alkylation of malonic and cyanoacetic esters. The monoalkylated product is obtained in 80–90% yield from 5.15 moles of diethyl malonate and 5.0 moles of n-butyl bromide in the presence of ethanolic sodium ethoxide prepared from 2.5 l. of ethanol and 5 gram atoms of sodium.

Diethyl Benzylmalonate.<sup>136</sup> If the standard alkylation procedure for malonic esters (cf. diethyl n-butylmalonate, above) is applied to a reactive halide such as benzyl chloride, diethyl benzylmalonate is obtained in 51-57% yield, the remainder of the product being diethyl dibenzylmalonate.<sup>119</sup> In the procedure of Leuchs an excess of diethyl malonate is used to reduce dialkylation (p. 122).

To an ethanolic solution of diethyl sodiomalonate prepared from 11.5 g. (0.5 gram atom) of sodium, 150 ml. of absolute ethanol, and 160 g. (1.0 mole) of diethyl malonate, is added dropwise, with stirring, 63.2 g. (0.5 mole) of benzyl chloride. The reaction mixture is boiled under reflux until it is neutral to litinus. After most of the ethanol has been distilled from the mixture under reduced pressure, water is added to the residual oil and the mixture is extracted with other. The other solution is dried and fractionally distilled. The diethyl benzylmalonate, collected at  $163-170^{\circ}/12$  mm., amounts to 107 g. (85%).

Diethyl Ethyl(phenyl)malonate (Inverse Addition Procedure).<sup>42</sup> In a 2-1, three-necked flask equipped with a dropping funnel, a mechanical stirrer, and an efficient reflux condenser connected to a trap chilled in solid carbon dioxide are placed 264 g. (1.1 moles) of diethyl phenylmalonate

<sup>171</sup> Norris and Tucker, J. Am. Chem. Soc., 55, 4697 (1933).

and 131 g. (1.2 moles) of ethyl bromide. While the contents of the flask are maintained at 45°, a solution of sodium ethoxide, prepared by the addition of 25 g. (1.1 gram atoms) of sodium to 450 ml. of absolute ethanol and followed by dilution of the solution with 10 ml, of ethyl acetate, is added dropwise with stirring. The sodium ethoxide solution is added at such a rate that the reaction mixture never becomes more than slightly basic to moist phenolphthalein paper. Near the end of the addition period any ethyl bromide which has collected in the solid earbon dioxide trap is returned to the reaction vessel. After the addition is complete (time required one and one-half to two hours) the reaction mixture is heated to 45° with stirring for one hour, and then the bulk of the ethanol is distilled from the reaction mixture. After water has been added to the residual oil and the mixture extracted with ether, the ether solution is dried over sodinm sulfate and fractionally distilled. The diethyl ethyl-(phenyl)malonate is collected at 166-168°/12-13 mm.; yield 248 g. (97%).

Diethyl Ethyl(isopropyl)malonate. (A) Alkylation of Diethyl Ethylmalonate. (A) Alkylation of Diethyl Ethylmalonate. (A) Alkylation of Diethyl Ethylmalonate, prepared from 24.8 g. (1.08 gram atoms) of sodium, 300 ml. of absolute ethanol, and 200 g. (1.08 moles) of diethyl ethylmalonate. 190 g. (1.12 moles) of isopropyl iodide is added dropwise. After the reaction mixture has been boiled under reflux with stirring for fifteen hours, most of the ethanol is distilled from the mixture and water is added. The product is extracted with ether, and the ether solution is dried over calcium chloride and fractionally distilled. The yield of diethyl ethyl(isopropyl)malonate, b.p. 230–235°, is 113 g. (46°,6). If the lower-boiling fractions are realkylated, the yield of diethyl ethyl(isopropyl)malonate may be raised to 75°...

diethyl ethyl(isopropyl)malonate, collected at 112-115°/18 mm., amounts to 150 g. (65%).

Diethyl Isopropyl(formamido)malonate.<sup>246</sup> Diethyl formamido-malonate<sup>572</sup> (11.5 g., 0.056 mole) is added in small portions to 1.44 g. (0.06 mole) of sodium hydride in 25 g. of anhydrous dimethylformamide. After the mixture has been allowed to stand for thirty minutes it is filtered and the filtrate is treated with 12.3 g. (0.10 mole) of isopropyl bromide. The resulting mixture is boiled under reflux for two hours, and then most of the solvent is removed by distillation under reduced pressure. The residue is mixed with 125 ml. of water and allowed to stand in an ice bath until the oil that initially separates has solidified. The crude product is eollected on a filter, washed with water, dried, and recrystallized from an ether-petroleum ether mixture. The yield of diethyl isopropyl(formamido)malonate, m.p. 67–73°, is 6.95 g. (50%). An additional recrystallization raises the melting point to 73.5–74°.

Diethyl 1,1-Cyclobutanedicarboxylate.<sup>573</sup> A solution of sodium ethoxide is prepared by the addition of 23 g. (1 gram atom) of sodium to 500 ml. of absolute cthanol contained in a three-necked flask equipped with a mechanical stirrer, a reflux condenser, and a long-stemmed dropping funnel. A 200-ml. portion of the solution is drawn into the dropping funnel with suction, and the dropping funnel is attached to the top of the reflux condenser. Diethyl malonate (96 g., 0.6 mole) is then added to the flask, and the mixture is heated to boiling with stirring. Over a period of one hour the sodium ethoxide solution and 101 g. (0.5 mole) of trimethylencbromide are added concurrently to the boiling reaction mixture. After the addition is complete the mixture is boiled under reflux with stirring for ninety minutes, and then about 400 ml. of ethanol is distilled from the reaction mixture. The residue is mixed with water and extracted with three portions of benzene. After the benzene has been distilled from the extract the residue is distilled under reduced pressure. The diethyl 1,1-eyelobutanedicarboxylate, collected at 105-112°/15 mm., amounts to 60-65 g. (60-67%).

Ethyl  $\alpha$ -Ethyl- $\alpha$ -methylvalerate. Ethyl  $\alpha$ -methylbutyrate (23.5 g., 0.18 mole) is added to an ethereal solution containing 0.18 mole of sodium triphenylmethide. After the reaction mixture has been shaken for five minutes, 30.7 g. (0.18 mole) of n-propyl iodide is added, and the reaction flask is stoppered, shaken, and allowed to stand overnight. The ethereal solution is washed with 200 ml. of water and dried, first over sodium sulfate and then over anhydrous calcium sulfate ("Dricrite"). After the other has been removed, the residue is distilled and the crude ester is

<sup>172</sup> Galat, J. Am. Chem. Soc., 69, 965 (1947).

<sup>273</sup> Cason and Allen, J. Org. Chem., 14, 1036 (1949).

of ethyl n-butyleyanoacetate. After the mixture has been stirred for five minutes, 73.8 g. (0.6 molc) of isopropyl bromide is added during a period of two minutes. The mixture is boiled under reflux with stirring for three hours, and then about 200 ml. of ethanol is distilled from the mixture under reduced pressure. The residue is diluted with 3 volumes of water, acidified by addition of a few drops of hydrochloric acid, and extracted with three portions of benzene. The combined benzene extracts are washed with water and distilled. The crude ester, b.p. 113-115°/6 mm., is shaken with 160 ml. of 5% aqueous sodium hydroxide for one and onehalf hours to hydrolyze any unchanged monoalkyl ester present. The ester is extracted with ether, and the extract is washed with water, diluted with benzene, and distilled. The pure ethyl n-butyl(isopropyl)cyanoacctate is collected at 115–116°/7 mm.,  $n_{\rm D}^{25}$  1.4327, yield 91.5 g. (87%).  $\alpha$ -Cyclohexylphenylacetonitrile. This Organic Syntheses procedure

illustrates the alkylation of a mononitrile in the presence of sodium amide. The reaction of a suspension in toluene of the sodium enolate of phenylacetonitrile (prepared in liquid ammonia from 0.35 mole of phenylacetonitrile and 0.35 mole of sodium amide) with 0.40 mole of cyclohexyl bromide produces  $\alpha$ -cyclohexylphenylacetonitrile in 65–77% yield.

#### TABULAR SURVEY OF THE ALKYLATION OF ESTERS AND NITRILES

The compounds listed in Tables I to XV have been arranged according to the nature of the active methylene compound. Malonic esters precede cyanoacetic esters, which in turn are followed by monocarboxylic esters and mononitriles. In Tables XVI to XX are surveyed several alternative methods of alkylation. Within each table the compounds are listed in order of increasing number of carbon atoms, monoalkyl derivatives preceding dialkyl derivatives. Among the monoalkyl derivatives acyclic groups are found first, followed in turn by saturated carbocyclic, aromatic, and then heterocyclic substituents. The straight-chain alkyl derivatives have been placed before branched-chain derivatives, the latter groups being listed in order of increased branching; the unsaturated substituents follow. Monocyclic precede bicyclic derivatives, the isomers with the smallest rings always being listed first. Oxygen heterocycles will be found before heterocycles containing sulfur. Next are listed the nitrogen heterocycles, followed by substituents containing two or more hetero

The alkylating agents employed have also been arranged in the order of increasing number of earbon atoms. Within a group of alkylating agents with the same number of carbon atoms the order of arrangement is

<sup>474</sup> Hancock and Cope, Org. Syntheses, 25, 25 (1945).

chlorides, bromides, iodides, unsaturated halides, carbonates, sulfates, sulfonates, dihalides, and epoxides. Ethers have been placed just after their hydrocarbon analogs. For example,  $n\text{-}\mathrm{C_3H_7O(CH_2)_3Br}$  would follow  $n\text{-}\mathrm{C_6H_{13}Br}$ , and p-methoxybenzyl bromide would follow p-methylbenzyl bromide.

In those reactions where more than one reference is eited the experimental data are taken from the first reference, the remaining references being arranged in numerical order. Where two figures are listed in the column headed "Yield" the first figure refers to the actual yield or conversion, and the second, enclosed in parentheses, is based on the amount of starting material consumed. In eases listed in the tables in which a compound resulting from hydrolysis, decarboxylation, or some other transformation was isolated rather than the initial alkylation product, the formula of the product actually isolated is listed and the yield eited is the yield of that compound. The literature has been reviewed through 1952 with the occasional inclusion of more recent work.

Because of the extent of the literature on alkylation and complexity of searching this literature by subject, there are undoubtedly many examples of alkylation that were not found. To avoid confusion in the nomenclature of disubstituted active methylene compounds with unlike substituents attached to the same carbon atom one of the groups is enclosed in parentheses. For example the ester  $C_2H_5C(C_0H_5)(CO_2C_2H_5)_2$  would be named diethyl ethyl(phenyl)malonate.

TABLE I

(The diethyl ester was used unless otherwise specified.) Alexelation of Malonic Esters, CH2(CO2R)2

Alsylating Agent Is	Product (C,H,O,C),CHCH(CO,C,Hs), (C,H,O,C),C==C(CO,C,Hs),	Yield, % 100	Bnso NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub>	Solvent Ethanol-ether Ethanol	Reference 260, 107, 261 260
G, CH,Br CH,I	CH,CH(CO,C,H3), CH,CH(CO,C,H3),	79-83 94	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ethanol Ethanol	570 169, 280, 577-582
CH,1 CH,1 (CH,).80,	CH,CH(CO,C,H,), CH,CH(CO,C,H,), CH,CH(CO,C,H,),	8	KOH Na NaOC <sub>1</sub> H <sub>5</sub>	None None Ethanol	82 583 336
p.CH,C,H,SO,CH,	cri,cri(co,c,ri,1), (c,ri,0,c),cricri,cri(co,c,ri,1),	80 09	NaOC,H, NaOC,H,	Ethanol Ethanol	335 293, 294
כוולן כווכו כווכן	(C,11,0,0),CHCH(CO,C,H,), (C,H,0,C),CHCH=C(CO,C,H,), (C,H,0,C),CHCH=C(CO,C,H,),	8# 20	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ethanol Ethanol	290, 291, 298 291, 584–587 588, 172, 589, 590
cti,vo, cti,vo, c,	$(C_1H_3O_1C)_1CHCH==C(CO_1C_1H_3)_2$ $(C_2H_3O_2C)_1CHCH(CO_2C_2H_3)_2$	1 1	NaOC2Hs NaOC2Hs	Ethanol Ethanol	591, 590 591, 590
C,H,Br C,H,Br C,H,I	C,H,CH(CO,C,H,), C,H,CH(CO,C,H,), C,H,CH(CO,C,H,),	80 90-94 83	Na NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	None Ethanof Ethanol	280 536, 545 399, 433, 540, 541, 592-594
Cılı,I	C,11,C11(CO,C,11,), and(C,H,),C(CO,C,H,),	I	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	595

THE ALKYLATION OF ESTERS AND NITRILES	165
596 56 82 96 280 597, 598 597, 598 596 249 220 335 268 600 601 602 603, 266 603, 266 602 604 484, 485, 488, 604 604	909
Ethanol Ethanol Nono Nono None None Nono C <sub>6</sub> H <sub>6</sub> Ethanol Ethanol Ethanol Ethanol Ethanol Ethanol	Ethanol
Mg(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Mg(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Mg(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Nn Nn NnOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>s</sub>
Good 60 Poor 75 100 100 100 68 68 68 	5-10
C,H,CH(CO,C,H,1) (C,H,1)+C(CO,C,H,1)+C,H,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,	CH <sub>2</sub> ClCH <sub>2</sub> OH  CH <sub>2</sub> CH <sub>2</sub> CCH <sub>2</sub> CH <sub>2</sub> O———CO  Note: References 577–1080 are on pp. 322–331.
C,H,I C,H,I	CH2CICH2OH Note: References 577-

TABLE I-Continued

Alkylation of Malonio Estens,  $\mathrm{CH}_2(\mathrm{CO}_2\mathrm{R})_2$  (The diethyl ester was used unless otherwise specified.)

Reference	909	909	606, 607	521	622	608 204, 542, 609 205 610
Solvent	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol Ethor Ethor C <sub>4</sub> H <sub>a</sub>
Baso	$ m NaOC_2H_{\it S}$	$ m NaOC_2H_5$	$\mathrm{NnOC_2H_5}$	$NaOC_2H_5$	$NaOC_2H_5$	$NaOC_2H_\delta$ $Na$ $Na$ $Na$
Xiold, %	5-10	5-10	ì	I	I	40 00 30
Product	0c0 CH2CH2CH2CH2	OCO CH2CH2CH2  CO	OC—O         CH2CH2CH2	0 $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$	$\alpha\text{-}Carbothoxybutyrolaetono$	None CII,OCH,CH(CO,C,H,s), CH,SCH,CH(CO,CH,s),* NCCH,CH(CO,Co,H,s),
Alkylating Agent	CH <sub>2</sub> BrCH <sub>2</sub> OH	CH,CICH,O,CCH,	CH,BrCII,O,CCII,	CH <sub>2</sub> —CII <sub>2</sub>	CII,—CII,	CH,CCI, CH,OCH,CI CH,SCH,CI CCH,CN

$C_3$					
n.C.H.Br	$n.C,H,CH(CO,C,H_5),$	80	$NaOC_2H_5$	Ethanol	611, 541
n.C.H.Br	n.C,H,CH(CO,C,H,),	80	Na	None	280
n.C.H.Br	(w.C.H.),C(CO,C,H.;),	30	NaOC,H5	Ethanol	612
n-C,H-1	n-C,H,CH(CO,C,H,),	ł	NaOC,H5	Ethanol	613, 50, 540
n-C.H-1	$n$ -C,H,CH(CO,C,H $\frac{\pi}{5}$ ),	ł	Zu	None	614
n-C,H,I	$(n-C,H_{\tau})_s C(CO,C_{r}H_{\bar{s}})_2$	33	NaOC,H5	Ethanol	612
n.C,H,I	(n.C,H,),C(CO,C,H,),	}	Zn	None	614
C,H,OCH,CI	(C,H,OCH,),C(CO,C,H,),	25	Na	Ether	542
C'H'SCH'CI	C2H,SCH2CH(CO2C2H5)2	ł	Na	Ether	205
	000				
$CH_3O(CH_2)_2I$	ch,ch,ch,ch,	40	$NaOC_2H_5$	Ethanol	909
	0000000				
$CH_3CH(OCH_3)CI$	$CH_3CH(OCH_3)CH(CO_2C_2H_5)_2$	70	Na	Ether	535
::C,H,Cl	¿.C,H,CH(CO,C,H,),	100	$NaOC_2H_5$	Ethanol	87
$i.\mathrm{C_3H_7Br}$	$i \cdot C_3H_i \cdot CH(CO_2C_2H_5)_2$	96	NaOC <sub>2</sub> H	Ethanol	169, 47, 387,
1					545
·CH,Br	$i \cdot \mathrm{C_3H_7CH(CO_2C_2H_5)_2}$	80	$NaOC_2H_5$	$(C_2H_5O)_2CO$	227, 51
::C3H,I	$i.c_3H,CH(CO_2C_2H_5)_2$	7.7	Na	None	280
.C.H.I	$i.\mathrm{C_3H_7CH(CO_2C_2H_5)_2}$	63	$NaOC_2H_5$	Ethanol	. 577, 569
Not stated	i-C <sub>3</sub> H,CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	09	$NaOC_2H_5$	Ethanol	540, 35, 571,
di maran					615
CH2=CHCH2BF	$CH_2 = CHCH_2CH(CO_2C_2H_8)_2$	16	$NaOC_2H_5$	Ethanol	121, 506, 571,
CH —CHCH B.	***				615-618
CH — CHCH B.	CH <sub>2</sub> =CHCH <sub>2</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	20	NaOC,H,	$(C_2H_5O)_2CO$	51
CH,—CHCH I	$(CH_2 = CHCH_2)_2 C(CO_2C_2H_5)_2$	Good	$Mg(OC_2H_5)_2$	Ethanol	56
CHCHCH 1	CH2=CHCH2CH(CO2C2H5)2	85	$NaOC_2H_5$	Ethanol	619
CII,=CHCH,I	$(CH_2 = CHCH_2)_2C(CO_2C_2H_5)_2$	100	$N_{8}OC_{2}H_{5}$	Ethanol	619
i e	$(CH_2 = CHCH_2)_2C(CO_2C_2H_5)_2$	ļ	$\mathbf{Z}_{\mathbf{n}}$	None	620
Note: References 577-1080 are on pp. 322-331.	aro on pp. 322-331.				

\* Dimethyl malonate was used in this experiment.

### TABLE I-Continued

Alkylation of Malonio Esters,  $\mathrm{CH_2(CO_2R)_2}$  (The diethyl ester was used unless otherwise specified.)

	Reference	102	285	621	699 400 400	693	623, 624	624	170,625	9.5	131, 136,	627-629 131, 172, 267,	630-632 573, 160, 172.	266, 483, 488, 491, 627, 633	336, 626	593. 634	593 593 635
	Solvent	Ethanol	Ethanol	Ethanol	Ethonol	-ether	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol		Ethanol	Ether	Ethanol CH <sub>3</sub> OH
	Baso	NaOC <sub>2</sub> H <sub>5</sub>	NaOCH3	$NaOC_2H_{\delta}$	NaOC.H	2	$NaOC_2H_5$	$N_BOC_2H_S$	$NaOC_2H_5$	$NaOC_2H_5$	NaOC2H 8	NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> Hs		NaOC <sub>2</sub> H <sub>5</sub>	Na	NaOC <sub>2</sub> H <sub>6</sub> NaOCH <sub>3</sub>
Yield,	%	34	52	26	93		62	8-10	55‡	38	70	15	60-65		ļ	70	20
	Product	NCCH2CH(CO2C2H5)2	F(CH <sub>2</sub> ) <sub>3</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	$/\text{ClCH} = \text{CHCH}_{2}\text{CH}(\text{CO}_{2}\text{C}_{1}\text{H}_{5})_{2}$	(\c)\c\frac{1}{1} \c\frac{1}{1} \cdot \c\frac{1}{1} \c\fra		[Cl(CH <sub>2</sub> ) <sub>3</sub> ] <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	Diethyl cyclobutano-I,l-dicarboxylate	Diethyl eyelobutane-1, I-dicarboxylate	1(CH <sub>2</sub> ) <sub>3</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	$\mathrm{Br}(\mathrm{CH}_2)_3\mathrm{CH}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	$(\mathrm{C}_2\mathrm{H}_3\mathrm{O}_2\mathrm{C})_2\mathrm{CH}(\mathrm{CH}_2)_3\mathrm{CH}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	Diethyl cyclobutane.1,1-dicarboxylate	носн	CH CCO2C2H5)2	CH,COCH,CH(CO,C,H,),	(CLA)OCHICH(CO,CLH); CH,COCH,CH(CO,CLH); CH,O,CCH,CH(CO,CH);*
Alkylating	Agent	P.CII,CeII,SO2CII,CH,CN	$F(\text{CH}_2)_3Br$	כוכוו≔כאכאימו	$Cl(CH_p)_3Br$		CI(CH <sub>2</sub> ) <sub>3</sub> Br	ClCH <sub>2</sub> / <sub>3</sub> Br	CI(CH) 1	Di(CI12)31	131 (C112)3DF	$\mathrm{Br}(\mathrm{CII_2})_3\mathrm{Br}$	$\mathrm{Br}(\mathrm{CH}_2)_3\mathrm{Br}$		$ m CH_3CHBrCH_3Br$	CH3COCH2Br	CH,COCH,Br CH,O,CCH,Cl

chichica cmi—chenica	$CH_{\beta}$ =:CClCH <sub>2</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> $\alpha$ .Carbethoxy. $\delta$ -chloro- $\gamma$ -valerolaetono	122	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ethanol Ethanol	636 136, 522
כווי–כונכווים	CICH,CHOHCH,CH(CONH,),	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	521
си, онсноиси, с	CH,OIICHOHCH,CH(CO,C,H,),	1	NaOC,H,	Ethanol	637
CH,BrCHBrCH,Br	$CH_2 = CBrCH_2CH(CO_2C_2H_6)_2$ and $(CH_2 = CBrCH_2)_2C(CO_2C_2H_6)_2$	I	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	638, 639
C.t n-C.H.Br	n.C,H,CH(CO,C,H,),	80-90	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	13, 121, 142, 540, 541, 640,
1.11.1.	".C.H.CH(CO.C.H.).	7.5	NaOC,H,	Ethanol	399, 141
1.C.H.OCH.CI	n.c.H.OCH,CH(CO,C.H.)	12	Na	Ether	542
15.1150.11.7	(n.C.H.OCH.),C(CO,C,H.),	ខ	Na	Ether	542
C.H.SO.(CH.), OC.H.	C,H,O(CH,),CH(CO,C,H,),	65	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	979
i.C.H.Br	¿C,H,CH(CO,C,Hs);	11	NaOC,H	Ethanol	427, 540, 555
					643
ACC-C411,Br	$sec. C_4H_sCH(CO_sC_2H_5)_2$	80-8I	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	14, 148, 540, 571, 643, 645
secC,H,Br	(*ec.C,H,),C(CO,G,H,-sec),;	78	NaOC,H,-sec	NaOC,H,.sec (sec.C,H,O),CO	51
Arc.C.II.	sec.C,H,CH(CO,C,H,s),	88	NaOC,H,	Ethanol	582
C11,C11(OC,11,)C1	CH,CH(OC,H,)CH(CO,C,H,),	28	NaNH,	C <sub>6</sub> H <sub>6</sub> -ether	203
CH,CH(OC,H,)Cl	CH,CH(OC,H,)CH(CO,C,II,),	27	Na	Ether	535
LC,111,13r	1.C,H,CH(CO,C,H5)2	9	NaOC,H,	Ethanol	15, 473
CH, CH = CHCH, CI	CH,CH=CHCH,CH(CO,C,H,),	50	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	18
CH,CH = CHCH,Br	CH,CH==CHCH,CH(CO,C,H,),	70	NaOC2H5	Ethanol	647, 648
Note: References 577-1080 are on pp. 322-331. • Dimothyl malonate was used in this experime   † The reactants were added in inverse order.	Nate: References 577-1080 are on pp. 322-331.  • Dimothyl malonate was used in this experiment.  † The reactants were added in inverse order.				
# Di-sec-butyl malonate	+ Di-src-butyl malonate was used in this experiment.				

18 To 5 73 5 2

TABLE I—Continued

Alexylation of Malonic Esters,  $\mathrm{CH_2(CO_2R)_2}$  (The diethyl ester was used unless otherwise specified.)

	Reference	647	18	G H	200	ć	649	į	431	481, 482	488, 308, 650		160	651	275	275	496, 498	541	494	125	126	636	533, 561, 652	021
	Solvent	Ethanol	Ethanol		Ethanol		Ethanol	,	Ethanol	Ethanol	Ethanol		Ethanol	Ethanol	Ether	Ethor	Ethanol	Ethanol	Ethanol	Tolueno	Tolueno	Ethanol	Ethanol	Ethanol
	Base	NaOC,H	NaOC <sub>2</sub> H <sub>5</sub>	4	NaOC <sub>2</sub> H <sub>5</sub>		NaOC2H;		$NaOC_2H_5$	$NaOC_2H_5$	NaOC2H3			NaOC <sub>2</sub> H <sub>5</sub>	Na	Na	NaOC2H5	NaOC2H5	$NaOC_2H_b$	$NaOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub>	NaOC2H5	NaOC2H6	NaOC.H.
Yield,	%	74	54	63	1		06-70		9	70	55		50-55§	58	69	l	56	I	65	1	55	41	ខ្ល	!
	Preduct	CH —CH/CH:), CH/CO.C. H.).	$(CH_{s}=CHCH(CH_{s})CH(CO_{2}C_{2}H_{s}))_{2}$	(CH,CH=CHCH,CH(CO,C,H,),	$CH_2 = C(CH_3)CH_2CH(CO_2C_2H_5)_2$	CH <sub>2</sub>	$\bigcirc$ CHCH2CH(CO2C2H3)2	ĊH <sub>2</sub>	CI(CH1), CH(CO,C,H5),	CICH, CH(CH,) CH, CH(CO, C, H,),	Diethyl eyclopentane.1,1.dicarboxylato	Diethyl 2-methylcyclobutane-1,1-	dicarbexylate	a-Carbethoxy-y-ethyl-y-butyrolactone	$(C_2H_5O_2C)_2C = CHCH_2CH(CO_2C_2H_5)_2$	$CICH_2CH(OC_2H_5)CH(CO_2C_2H_5)_2$	Diethyl tetrahydropyran-4,4-diearboxylate	$[\mathrm{CH}_2 = \mathrm{CHO}(\mathrm{CH}_2)_2]_2 \mathrm{C}(\mathrm{CO}_2 \mathrm{C}_2 \mathrm{H}_5)_2$	Diethyl tetrahydropyran-4,4-dicarboxylate	$(n\text{-}\mathrm{C}_3\mathrm{H}_7\mathrm{SCH}_2)_2\mathrm{C}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	$\{C_2H_5\mathrm{SCH}(\mathrm{CH}_4)\mathrm{CH}(\mathrm{CO}_2G_2H_5)_2 \text{ and } \{[C_2H_5\mathrm{SCH}(\mathrm{CH}_4)]_2\mathrm{C}(\mathrm{CO}_2G_2H_5)_2 \}$	CICH==CHCH(CH3)CH(CO2C2H3)2	CH3CCI=CHCH2CH(CO2C2H3)2	(C2H5O2C)2CHCH2CH==CHCH2CH(CO2C2H5)2
A Handa Line	Ancytating	OH CHOTH B-		CH2=CHCH(CH3)CI	$CH_2 = C(CH_3)CH_2Br$	CH,	CHCH2Br	CH,	Cl/CH,),Br	CICH, CH(CH,)CH, Br	Br(CH,),Br	CH, CHBr(CH,), Br		C,H,CHOHCH,Cl	C'H'OCHCICH'CI	C,H,OCHCICH,CI	$CI(CH_2)_2O(CH_2)_2CI$	$CH_2$ = $CHO(CH_2)_3$ CI	$I(CH_2)_2O(CH_2)_2I$	n-C <sub>3</sub> H,SCH <sub>2</sub> Cl	$C_2H_5SCH(CH_3)CI$	CH <sub>3</sub> CH=CHCHCl <sub>2</sub>	CH3CCI=CHCH2CI	BrCH;CH=CHCH2Br

$BrCH_2CH = CHCH_2Br$	$(C_2H_2O_2C)_2$ CHCH $(CH=CH_2)$ .	١	H DOON	Ethunol	06
BrCH2CH=CHCH3Br	$CH_1 = CHC - C(CO_2C_2H_3)_2$ $CH_4 = CHC - C(CO_4C_2H_3)_2$	26	NaOC2H 5	Ethanol	00
CH2=CHCH-CH2	α-Carbothoxy-γ-vinyl-γ-butyrolaetone	73	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	11, 526
CH <sub>3</sub> OCH <sub>2</sub> CH—CH <sub>2</sub>	CH,OCH,CH—CH,CH,	09-09	60-60 NaOC <sub>2</sub> H <sub>3</sub>	Ethanol	524
CI(CH <sub>2</sub> ),CN	$NC(CH_2)_3CH(CO_3C_2H_3)_2$	7.5	NaOC, H.	Ether	132
CICH, CO, C, H,	C.H.O.CCH,CH(CO.C.H.),	1	Na	Ether	653
CICH,CO,C,H,	C,H,O,CCH,CH(CO,C,H,),	I	Na	$C_{\mathbf{k}}\mathbf{H}_{\mathbf{k}}$	653, 161, 654
CICH,CO,C,H,	$C_2H_5O_2CCH_2CH(CO_2C_3H_5)_2$	67	NaOC,H,	Ethanol	655, 594, 635
CICH, CO, C, H,	(C2H3O2CCH2)2C(CO2C2H3)2	87	Mg(OC,Hs),	Ethanol	555
4-Culorometnylimidazole hydrochloride	Diethyl (4-imidazolemothyl)malonato	67-	NaOC,H,	Ethanol	209
$C_{\mathfrak{s}}$					
$n$ ·C $_{ m s}{ m H}_{ m I1}{ m Br}$	$n$ -C $_5\mathrm{H}_{11}\mathrm{CH}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	70-85	70-85 NaOC2Hs	Ethanol	545, 148, 543,
CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>4</sub> Br	CH3O(CH2),CH(CO2C2H5)2	80-84	NaOC,Hs	Ethanol	66 <u>9</u> 66 <u>9</u>
$^{1-\mathrm{C}_5\mathrm{H}_{11}\mathrm{Br}}$	$i$ ·C $_{5}$ H $_{11}$ CH(CO $_{2}$ C $_{2}$ H $_{5}$ ) $_{2}$	7.8	NaOC,H,	Ethanol	657, 35, 148,
n·C,H,CH(CH <sub>3</sub> )Br	n-C <sub>3</sub> H,CH(CH <sub>3</sub> )CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	19	NaOC, II,	Ethanol	540, 545, 555, 571, 616, 658 148, 659
i.C.H.(CH.).Br	sec-C,H,CH,CH(CO,C,H,),	70-85	NaOC, H,	Ethanol	545, 659
(C,H,),CHBr	Canada (CHallach (CO3H))	83	NaOC, Hs	Ethanol	138
Nete Butham	12211512 CACA(CO2C3H5)2	36	NaOC, II,	Ethanol	148
§ The product contained up to 18% of unsatural I The eyanide group has —CHN.	§ The product contained up to 18% of unsaturated material.    The cyanide group has = C'18.				

'FABLE 1-Continued

ALKYLATION OF MALONIC ESTERS, CH<sub>2</sub>(CO<sub>2</sub>R)<sub>2</sub>

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		Yiold,	,	Solvent	Reference
Alkylating	Deschoot	%	13030		ago
Agent	THU COMMON THE COMMON	١	NnOC,H5	Ethanol	900
(-F).CH,CH-=CHCH(CH2)CI	rac.CII, CHCIICII(CIII,)CII(COLCI-15)?	t	NaOC2H,	Ethanol	666, 47, 616,
CII, CH(CH,),Br	$CH_{s} = CH(CH_{s})_{s} CH(CO_{s}C_{s}H_{s})_{s}$	7.0	NaOC2H5	Eliano	663
(CII,),C=CHCH,Br	(0113)2	ij	NoOC.H.	Ethanol	664
116200(011,),01	$HC = CC(CH_s), CH(CO, C, H_s), CH(CO, C, H_s)$	ĵ l	NaOC,H,	Ethanol	304 308,
Br(CH <sub>2</sub> ) <sub>3</sub> Br	Diethyl cyclohoxano-I, I. dicarboxylate	30			
	Diethyl 2.methyleyelopentane.I, I-	١	NaOC,H,	Ethanol	665
Dr(C112)3-011(C113)3-01	dicarboxylate	56	NaOC,H,	Ethanol	318, 173, 616
	(CH <sub>3</sub> ), C=CHCH <sub>2</sub> CH(CO <sub>3</sub> C <sub>2</sub> II <sub>5</sub> );	}			199
(CII,),CBr(CII,),Br	(C2H,O2C),CHCH(CO2C2H5)2	7.4	NaOCH3	Ethanol	285
F(CH,)3Br	$F(CH_2)_5CH(CO_2C_3H_5)_2$	56-59	NaOC2H &	Ethanol	899
NC(CII,),Br	NC(CH <sub>3</sub> ),CH(CO <sub>2</sub> C <sub>2</sub> M <sub>3</sub> )2	1	Na	١	101
CH.CHBrCO,C.H.	C,H,O,CCH(CH,)CH(CO,C,H,S)	50	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	223, 669
CH, CITBrCO, C, H,	C,H,O,CCH(CH3)CH(CO,C,h,S)2	538	NaOC,H;	Ethanol	610, 670
Br(CH,),CO,C,H,	CH OCCONTO	28	NaOC2H5	Ethanol	671
Br(CH,),CO,C,H,	$\{C_1H_sO_2C\{CH_2\}_2^2\}_2^2C\{CO_2C_2H_s\}_2^2$	28	H OC.	Ethanol	672
1/CH ), CO. C. H.	[C,H,O,C(CH,),1,C(CO,C,H,),	1	IN BOOGITE		
2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 -	CHCO,C,H,				1
on B. Cub.Co C. H.	CH <sub>2</sub> —C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	77	NaOC <sub>2</sub> H <sub>3</sub>	Ethanol Ethanol	673 674
Br.C=CHCO,C.H.	Not ostablished	FOOL	3116001118		

		ì	Na OCEL	CH,OH	675
B.CH/CO CH )	(CH <sub>3</sub> O <sub>2</sub> C) <sub>2</sub> CHCH(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> *	,,,,	5		
DIOII(0020113/2	((CH <sub>3</sub> O <sub>3</sub> C) <sub>2</sub> CHC(CO <sub>3</sub> CH <sub>3</sub> ) <sub>2</sub> CH(CO <sub>3</sub> CH <sub>3</sub> ) <sub>2</sub>	202	NuOC,H;	Ethanol	334
Cyclobutylnethyl tosylate	Diethyl (ey clobary moonly)	20	NaOC,H,	Ethanol	31, 148, 677
Cyclopentyl broining	Diethyl evelopentylmalonato	20	NaOC,H,	Ethanol	929
Cyclopenty Lourne	Diethyl 2-evelonentenylmalonato	20	Na	C,H,	287
2-Cyclopentenyl enloride	Diethyl 2-cyclopentenylmalonate	70	Na	Tolucue	678, 151
2-Cyclopentenyl chlorido	Dictlyl 2-cyclopentenylmalonate	84-88	NnOC2H3	Ethanol	274, 286, 287, 679-681
	[ Diethyl bicyclo-[3.1.0]-hex-2-eno-6,6-		;		
	diearboxylato	£	NaOC, H,	Ethanol	152
trans-1,4-Dibromo-2. cyclopentene	Diethyl (ethoxycyclopentenyl)malonato (isomers)	*			
	(c,H,0,0,0),Hc \co,c,H,),	l			
cis.1,4.Dibromo.2.	Diethyl bicyclo-[3.1.0]-liex-2-ene-6,6-				
cyclopenteno	dienrboxylate	16	NnOC,H,	Ethanol	152
C,H,OCH,CH—CH,	C,H,OCH,CHCH,CHCO,C,H,	20-60	NnOC,H,	Ethanol	524
ò	000				
H,C,C(CH,)—CH,	H,C,C(CH,)CH,CHCO,C,H,	20-60	50-60 NaOC, Hs	Ethanol	526
\	030				
Cyclopenteno oxide	trans-Diethyl (2-hydroxy-				
	eyclopentyl)malonato	52	Na	$C_{f e}H_{f e}$	t-
Cyclopentene oxide	trans-Diethyl (2-hydroxy-				
	cyclopentyl)malonato	70-75	NaOC,H,	Ethanol	1~
Tetrahydrofurfuryl bromide	Dicthyl tetrahydrofurfurylmalonate	70	NaOC,H,	Ethanol	685
Furfuryl chloride	Diethyl furfurylmalonate	92	NaOC,H,	Ethanol	244
2-Chlorotetrahydropyran	Diethyl 2-tetrahydropyranylmalonate	ł	NuH	Toluene	683
Note: References 577-1080 are on pp. 322-331.	0 aro on pp. 322-331.				

water the same and place.

\* Dimethyl malonato was used in this experiment.

## TABLE I-Continued

Alkylation of Malonic Esters,  $\mathrm{CH}_2(\mathrm{CO}_2\mathrm{R})_2$  (The diethyl ester was used unless otherwise specified.)

Reference	282, 538	151	684	685	169	616	989	138	555	32	282, 555, 687,	688	689	009	66 66		695	693	510	169	169	•	<b>7</b>
Solvent	Ethanol	Ethanol	Ethanol	n.C,H,OII	. !	Ethunol	Pthanol	Ethnnol	Ethanol	Ethunol	Ethunol		Ethnool	Ethanol	Ethanol	Ethanol.	toluene	ì	Ethonol	Ethanol	Ethnnol	,	Ethanol
Baso	NaOC.II.	NAOC. II.	V.,OC.11.	KAOC.H.		VanOC II	XaOC:11.	NaOC. II.	Kacci.H.	KnOC, 11.	ChOC.H.	, , ,	NaOC.11.	NuOC, II,	NnOC,115	NnOC,113	•	Not stated	NaOC, II,	NnOC. H.	Mg(OC, 113),		NnOC, II,
Yield,	2.0	60.00	1 6	6 6	1 3	1 1	100	ĉ	5	3 13	50-03	10-00	17	20	\$	:3	•	100		15	· #1	91	-
Product		$n.C_6H_{13}CH(CO_2C_2H_6)_2$	$(n\cdot \operatorname{C}_{\mathfrak{s}}\operatorname{H}_{11})_{\mathfrak{s}}\operatorname{C}(\operatorname{CO}_{\mathfrak{s}}\operatorname{C}_{\mathfrak{s}}\operatorname{H}_{\mathfrak{s}})_{\mathfrak{s}}$	n.C,H13CH(CO,C,H5)2	$(n.C_6H_{13})_2C(CO_2C_2II_5)_2$	$CH_2O(CH_2)_3CH(CO_2C_2H_3)_2$	C, H, O(CH2), CH(CO, C, H, s);	n.C,H,CH(CH3)CH(CO2C3H3)2	i.C,H,(CH2),CH(CO,C,H3),	n.C,H,CH(CH,)CH,CH(CO,C,H,S)2	n.C,H,CH(C,H,)CH(CO,C,H,S)2	(C,H,),CHCH,CH(CO,C,H,s);	( If o Collin House to as an	(C <sub>1</sub> H <sub>2</sub> O) <sub>2</sub> CHCH <sub>2</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> ) <sub>2</sub>	CC119(CH2)2CH(CC1C1H3/2	C2H3C11(CC113)(C112);C11(CC1C113);	C,H,CH = CH(CH,); CH(CO,)	TO THE CHICAL STREET			CH <sub>3</sub> O(CH <sub>3</sub> ), CH <sub>3</sub> CH CH <sub>3</sub> CH (CO <sub>3</sub> C <sub>3</sub> CH <sub>3</sub> S)	CH3O(CH3)/2CH==CHCHCHCCCCCCCCCCTCT);	CH3O(CH3), CH=CHCH, CH(CO,C,H3),
Alkylating Agent	$C_{\rm e}$	n.C.H.,Br	n.C.HBr	n.C.H1	".C. HI	CH O(CH-).Br	C.H.O(CH.),Br	n.C,H,CH(CH3)Br	i.C,H,(CH,),I	n.C,H,CH(CH,)CH,Br	n.C,H,CH(C,H,)Br	(C,H,),CHCH,Br		$(C_2H_2O)_2CHCH_2Br$	t.C,H,(CH2),Br	C,H,CH(OCH,)(CH,),CI-IXI	trans-C2H3CH=CH4(CH2)2Br		cis-C <sub>2</sub> H <sub>3</sub> CH=CH(CH <sub>2</sub> ) <sub>2</sub> 1	CH <sub>2</sub> =CH(CH <sub>2</sub> ) <sub>4</sub> I3r	CH,O(CH,),CH=CHCH,CI	CH,O(CH,),CH=CHCH,Cl	CH,O(CH,),CHCICH=CH,

	$(CH_1O(CH_2)_3CH \rightleftharpoons CHCH_2CH(CO_2C_2H_5)_2$	29	$Mg(OC_2H_5)_2$	Ethanol	694
CH,O(CII,),CHCICH=CH,	$ \{ [\text{CH}_3\text{O}(\text{CH}_1)_2\text{CH} = \text{CHCH}_1]_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2 \\ \text{$[n.\text{C}_3\text{H}_7\text{C} = \text{CCH}_1]_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$} \\ \text{$[n.\text{C}_3\text{H}_7\text{C} = \text{CCH}_1]_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$} \\ \end{array} $	5 57 13	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	695
CH3CHBr(CH2)4Br	Totraothyl 2-mothylheptane-1,1,7,7- tetracarboxylato Diethyl 2-methylcylcohexane-1,1-	1	NaOC2H5	Ethanol	969
CH,CHBr(CH,),Br Br(CH,),Br	(dicarboxylate CH <sub>3</sub> CHBr(CH <sub>2</sub> ),CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Dicthyl cycloheptane 1,1 dicarboxylate and	1 1 1	NaOC2Hs NaOC2Hs	Ethanol Ethanol	210 269
$C_2H_3C(CH_3)Br(CH_2)_2Br$	tetracthyl octano-1,1,8,8-tetracarboxylato (C2H5,02C),CHCH(CO,C2H5), and CHCH(CHCHCHCHC) CH	1	NaOC <sub>2</sub> H,	Ethanol	697, 318
CH,CO(CH,),Br (CH,),N(CH,),CH(CH,)Cl	CH,CO(CH,),CH(CO,C,H,), CH,V.V.CH,.),CH(CH,V.V.CH,CO,C,H,),	44.	NaOC.H.	Ethanol Ethanol	698
(C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> N(CH <sub>3</sub> ) <sub>3</sub> Cl	(C,H,,),N(CH,,),CH(CO,C,H,s),	45	Na	C,H,	610
Br(CII2), CN	NC(CH2), CH(CO2C2H5)2	83	NaOC,H,	Ethanol	700
C,H,CHBrCO,C,H,	C,H,O,CCH(C,H,)CH(CO,C,H,),	ļ	Na	None	161
C,H,CHBrCO,C,H,	C,H,O,CCH(C,H,)CH(CO,C,H,S),	55	NaOC2H5	Ethanol	223
(CH <sub>3</sub> ) <sub>2</sub> CBrCO <sub>2</sub> C <sub>2</sub> H <sub>3</sub>	C,H,O,CC(CH,),CH(CO,C,H,S),	1	Na	None	161
(CH <sub>3</sub> ),CBrCO,C,H,	C <sub>2</sub> H,O <sub>2</sub> CC(CH,) <sub>2</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CHCO <sub>2</sub> CH,	09	$NaOC_2H_b$	Ethanol	701, 223, 702
CH,O,CCHBrCHBrCO,CH, Cyclohexyl bromide	CH,0,CCH—C(CO,CH,),* Diethyl cyclohexylmalonate	80–90 60	NaOHC3 NaOC2H5	Methanol Ethanol	175, 703 35, 31, 50, 149, 286, 704,
Cyclohexyl bromido Di-t-butyl cyclohexyl I-Chloro-2-cyclohexen Diethyl 2-cyclohexen,  Note: References 557-1080 are on pp. 322-331.  * Dimethyl malonate was used in this experiment.  ¶ Di-t-butyl malonate was used in this experiment.	Di-t-butyl cyclohoxylmalonate¶ Diethyl 2-cyclohoxenylmalonato aro on pp. 322-331. sed in this experiment. sed in this experiment.	7.7	NaH  -	.С <sub>4</sub> Н <sub>9</sub> ОН —	705 393 150

# TABLE I-Continued

Alkylation of Malonic Esters,  ${\rm CH_2(CO_2R)_2}$  (The diethyl ester was used unless otherwise specified.)

Reference 150 150 287, 150, 286, 706	706 706	8, 707 50, 708, 709 710 710	139, 284 711 184, 712 713, 714	715	714	327, 326, 328
Solvont Ethanol Ethanol Ethanol	Ethanol Ethanol	Ethanol Ethanol Ethanol	Ether Ethanol Ether	Ether	Ether	Ethanol. C <sub>6</sub> H <sub>6</sub>
Baso NaOC <sub>2</sub> H <sub>s</sub> NaOC <sub>2</sub> H <sub>s</sub>	$NaOC_2H_b$ $NaOC_2H_b$	NaOC2H5 NaOC2H5 — NaOC2H5	Na NaOC2H5 NaOC2H5 Na	Na	Na	40 (53) NaOC <sub>2</sub> H <sub>6</sub>
Yield, % <60 ca. 40 66	111	× × × × × × × × × × × × × × × × × × ×	90     63	90	1	40 (53)
Product Dicthyl 2-cyclohexenylmalonato Dicthyl 2-cyclohexenylmalonato (Diethyl 2-cyclohexenylmalonate	\\ \left(C_1H_sO_2C)_2CHCH(CO_2C_2H_s)_2\\ \text{Diethyl (2-hydroxycyclohoxyl)malonato}\ \text{Lactone from 2-hydroxycyclohoxylacetic acid}\end{align*}	Lactone from diethyl (2-hydroxy- cyclohexyl)malonato Diethyl [β-(2-thienyl)ethyl]malonate None Di-(1-nitroso-4-piperidylmethyl)malonie aeid	Diethyl (2,4-dinitrophenyl)malonato Diethyl (2,4,6-trinitrophenyl)malonate Diethyl (2,4-dinitrophenyl)malonato Diethyl (2,6-dinitro-4-chlorophenyl)malonato	Diethyl (2,6-dinitro-4-bromophonyl)malonato	Dimethyl (2,4-dinitro-3,5-	dichlorophenyl)malonato* Diethyl (2,4-dinitro-5-bromophenyl)malonate
Alkylating Agent 1,2-Dichlorocyclehexane 1.Chlore.2-bromocyclohexane	1,2.Dibromocyclohexane Cyclohexene bromolydrin	Cyclohexene oxido Gyclohexene oxido β.(2.Thionyl)ethyl elilorido 4.Bremomethylpiperidine 1.Nitroso-4.bromo-	methylpiperidine 2,4.Dinitrochlorobenzene Pieryl chloride 2,4.Dinitrobromobenzene 2,5.Diehloro-1,3-dinitro-	benzene 1-Chloro-4-bromo-2,6-	dinitrobenzene 2.4.Dinitro-1,3,5.	trichlorobenzene 2,4-Dinitro-1,3,5-tribromobenzeno

".C,11,0CH,CH—CH,	$n.\mathrm{C_3H},\mathrm{OCH_2CHCH_2CHCO_2C_2H_5}$	20-60	50-60 NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	524
.C,11,0CH,CH—CH2	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	50-60	50-60 NaOC2H5	Ethanol	524
,:C,H,C(CH,)—CH <sub>2</sub>	o	50-60	50-60 NaOC <sub>2</sub> H <sub>s</sub>	Ethanol	525
$G_{\gamma}$ $n.C_{\gamma}H_{1s}Br$ $C_{2}H_{1s}O(CH_{1s})_{3}Br$	n-C,H <sub>1s</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>5</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	82 76	NaOC <sub>2</sub> H <sub>6</sub> NaOC <sub>2</sub> H <sub>6</sub>	Ethanol Ethanol	656, 282
CH3CO2(CH2)5Cl-NaI	$^{\mathrm{CH_{2}(CH_{2})_{1}CHCO_{2}C_{2}H_{5}}}$	i	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	717
I,(CH2),H30;	O	ł	NaOC,H,	Ethanol	138
i.C,H,,CH(CH,)I	¿.C,H,1,CH(CH,)CH(CO,C,H,)2	21	$NaOC_2H_5$	Ethanol	718
:CH,CH(CH,)CH,Br	i.C,H,CH(CH3)CH2CH(CO2C2H5)2	62	$NaOC_2H_5$	Ethanol	989
1.C,11,(CH,)3Br	6.C,H,(CH2),CH(CO2C2H5)2	58	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	069
C,H,CH(CH,)CH(CH,)CH,Br	C2H3CH(CH3)CH(CH3)CH2CH(CO2C2H3)2	7.0	$NaOC_2H_5$	Ethanol	989
n.C,H,CH(CH,)CH(CH3)Br	$n \cdot C_3 H_1 CH(CH_1) CH(CH_1) CH(CO_2 C_2 H_5)_2$	15	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	989
$(C_2H_5)_2CBr(CH_2)_2Br$	$(C_2H_5)_2C$ =CHCH $_2$ CH $(CO_2C_2H_5)_2$ and $(C_2H_5O_2C)_3$ CHCH $(CO_3C_3H_5)_3$ .	1	NaOC <sub>2</sub> H 5	Ethanol	697, 318, 667
	$(\operatorname{BrCH}_2\operatorname{CH}(\operatorname{C}_4\operatorname{H}_3\cdot n)\operatorname{CH}_2\operatorname{CH}(\operatorname{CO}_2\operatorname{C}_2\operatorname{H}_5)_3$	41	NaOC,H,	Ethanol	489
$n \cdot \mathrm{C}_{\mathbf{t}} \mathrm{H}_{\mathbf{b}} \mathrm{CH}(\mathrm{CH}_{2} \mathrm{Br})_{\mathbf{z}}$	Diethyl 3.n-butyleyelobutane-1,1-diearboxylate	24			
Chloropentamethylethane	(C,H,O,C),CHCH(CO,C,H,)),	1	NaOC,H	Ethanol	719
CII, CH(CH2), Br	$CH_2 = CH(CH_2)_s CH(CO_s C_2 H_5)_s$	98	$NaOC_2H_5$	Ethanol	661
$n \cdot C_i H_i C = CCH_2 Br$	$n \cdot C_4H_4C = CCH_4CH(CO_2C_2H_5)_2$	99	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	695
CH, CHBr(CH,), CO, C, Hs	$C_2H_5O_2C(CH_2)_2CH(CH_3)CH(CO_2C_2H_5)_2$	Poor	$NaOC_2H_5$	Ethanol	720
Note: References 577-1080 are on pp. 322-331.	) aro on pp. 322–331.				

Dimethyl malonato was used in this experiment.

### TABLE I—Continued

Alkylation of Malonic Esters,  ${\rm CH}_2({\rm CO}_2{\rm R})_2$  (The diethyl ester was used unless otherwise specified.)

Reference	668 223 721	722 675 723, 168	724 725 726	727	108	704 150 147	720
Solvent	Ethanol-C <sub>6</sub> H <sub>6</sub> Ethanol	Ethanol Ethanol Ethanol	Xyleno Ethanol Xyleno	Ethanol	1	Ethanol Ethanol —	Ethanol
Baso	NaOC2H5 NaOC2H5 Na	NaOC2H5 NaOC2H5 NaOC2H5	Na NaOC <sub>2</sub> H5 Na	NaOC2H3	1	NaOC2H3 NaOC2H3 Na	NaOC <sub>2</sub> H <sub>5</sub>
Yield, %	84 38 64	\ \ \	09-09	1	02-00	11 1 8	Good
Product	$C_2H_sO_2C(CH_2)_4CH(CO_2C_2H_3)_2$ $C_3H_sO_2CCH(C_3H_7\cdot i)CH(CO_2C_2H_3)_2$ $C_2H_sOCH_2CHCO_2C_2H_3$	C2H(CO2C2H3); (C2H,O2C);CHCH(CO2C4H3); (C2H,O2C);CHCH(CO2C4H3); CH3COCHCH(CO2C4H3);	CH2CO2C2H5 Diethyl (\$\theta\coperate Coperate Co	Dicthyl [ $eta$ -(2-cyclopentenyl)othyl]malonato	Diethyl (y.tetrahydro- furfurylpropyl)malonate	Diethyl (cyclohexylmethyl)malonato Diethyl (1-methyleyclohexyl)malonato	Diethyl (2-methyleyelohexyl)malonaco (Diethyl (3-methyleyelohexyl)malonato (cis and trans isomors) (Diethyl di-(3-methyleyelohoxyl)malonato
Alkylating	$\Lambda_{\rm BCH}$ $Br({\rm CH_2})_{\rm t}{\rm CO_2}C_2{\rm H_3}$ $i\cdot C_3{\rm H_3}{\rm CH_2}{\rm CH_5}$ $C_2{\rm H_3}{\rm CO_2}C_2{\rm H_3}$	CICH(CO,C,H,), BrCH(CO,C,H,), CH,COCHBrCH,CO,C,H,	eta-Cyclopentylethyl bromide $eta$ -Cyclopentylethyl bromido $eta$ -Cyclopentylethyl bromido $eta$ -Cyclopentenyl)ethyl	bromide $\beta$ .(2.Cyclepentenyl)ethyl $\frac{\beta}{\lambda}$	u-Commue $ u$ -Tetrahydrefurfurylpropyl bremide	Bremomethylcyclohexane 1-Methylcyclohexyl chlorido	2-Methylcyclohexyl bromide 3-Mothylcyclohexyl bromido

352 149 362	150	150, 730	730	150	150	393 83 136, 107, 108, 113, 119, 121.	142, 411, 430, 433, 571, 732,	734, 735	733	56	736, 737	115	738	
Ethanol Ethanol Ethanol	Ethanol	Ethanol	Ī	Ethanol	Ethanol	cc <sub>4</sub> H <sub>5</sub> OH CH <sub>5</sub> CH(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Ethanol			Ethanol	Ethanol	Ethanol	Ethanol	I	
NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC.H.	NaOC,H,	1	NaOC,H,	NaOC <sub>2</sub> H <sub>3</sub>	NaH KOH NaOC <sub>2</sub> H <sub>5</sub>			NaOC,H.	$Mg(OC_2H_3)_2$	NaOC,H,	NaOC,Hs	1	
9   13	1	1	1	[	1	80 85		12	8-1-87	1	76	32	20	
Diethyl (3-methyleyelohexyl)malonato Diethyl (4-methyleyelohexyl)malonato Diethyl (4-methyleyelohexyl)malonato	CH(CO,C,H,),	Diethyl (2-methyl-2-cyclohexenyl)malonato	Diethyl (5-methyl-2-cyclohexenyl)malonato	Two products, no analyses given	Structure of product not determined	C,11,CH,CH(CO,C,H,), C,11,CH,CH(CO,C,H,), (C,H,CH,CH(CO,C,H,),		\(c,11,c11_);C(CO,C;H_));	(C,11,CH,),C(CO,C,11,),	(C,II,CII,),C(CO,C,H,),	{	/m.ClC,H,CH;CH(CO,C,H,), /m.ClC,H.ClL,C(CO,C,H,),	(p-ClC, II, CH, CH(CO, C, H, ); (p-ClC, II, CH, CH(CO, C, H, );	) are on pp. 322–331.
z.Methyleyelohaxyl iodido t.Methyleyelohaxyl bromido 4.Methyleyelohaxyl iodido	1.1Fromomethyl 1.bromocyclobexano	1-Methyl-1,2-dibromo-	Cyclopexano CMethyl-1,2-dibromo-	(+).5:Methyl-1,2.	dintennery Conexado 1.Cyano.1,2 dibromo.	อำเวนา อำเวนา	e,u,en,en		CHOLO	Catania	o.CTC.H.CH.CI	m-ClC,H,CH,Cl	$p$ -ele, $H_i$ e $H_i$ el	Nefe: References 577-1080 are on pp. 322-331.

# TABLE I-Continued

Alkylation of Malonic Esters,  $\mathrm{CH_2(CO_2R)_2}$  (The diethyl ester was used unless otherwise specified.)

T) - C	Iverorouse	406	738	391	739	112, 740, 741		342		117		342	611 811	740-742		712	86	59.4	1	525	
	Solvent	Ethanol	Ethanol	Ethanol	CHOH	Tthonal	TO IMPRINGT	CHOH	7176117	Tthanol		CH OH	Tallera	Ethanoi		Rther	Tethonol	Pthonol	Edunoi	Ethanol	
	Baso	NAOC.H.	NaOC2H2	H JOAK	NAOC2115	NAOCH3	NaOC2II s	1100-75	NACCES 3	TI NO II	Naccens	TIVO TI	INCOLLS	NaOC <sub>2</sub> H 5		N.	Na Noor		NaOCzHs	NoOCH.	9442
Yiold,	%	Cool	1000	;	40	;	10	46	١		l		!	00	91	9	l	١	20-60	000	00-00
	Product		o.BrC,H,CH <sub>2</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>6</sub> ); (n.BrC,H.CH,CH(CO,C <sub>2</sub> H <sub>5</sub> );	(p. BrC,H,CH,2),C(CO,C,H,5),2	"IC,H,CH,CH(CO,C,H,)	(0.0,NC,H,CH2)2C(CO2CH3)2*	(0.0,NC,H,CH,CH(CO,C,Hs))	$(0.0_2^{\circ} \mathrm{NC_6H_4^{\circ} CH_2})_2^{\circ} \mathrm{C}(\mathrm{CO_2^{\circ} C_2^{\circ} H_3})_2^{\circ}$	m.O,NC,H,CH,CH(CO,CH3),* and	(m.02NC,H,CH2)2C(CO2CH3)2*	$m.0_2 \mathrm{NC_6H_4CH_2CH(CO_2H)_2}$ and	$(m.0_2\mathrm{NC_6H_4CH_2})_2\mathrm{C}(\mathrm{CO_2C_2H_5})_2$	p-0,NC,H,CH,CH(CO,CH <sub>3</sub> ),*	$(p \cdot \hat{O}_2 NC_6 H_4 CH_2 CH(CO_2 C_2 H_5)_2$		((p-02NC,H,CH2)2C(CO2C2H5)2	Dimethyl (2-nitro-4-eyanophenyl)malonato	Diethyl (o-earboxyphenyl)malonato	$n.C_i$ H,OCH $_2$ CHCH $_2$ CHCO $_2$ C $_2$ H $_3$		$n.C_1H_{\bullet}C(CH_3)CH_2CHCO_2C_2H_{\bullet}$
	Alkylating	Agent	o.BrCgH,CH2Cl	$p.\mathrm{BrC_6H_4CFI_2Br}$	TO II OIL B.		0.021100111011301	$o.O_2\mathrm{NC}_0\mathrm{H_1CH_2Cl}$	D'HO H ON O	11: (11: (0:11) (0:12) (11: (11: (11: (11: (11: (11: (11: (11	".O.NG.H.CH.CI	22-10-21-0	**X*HUH'UN'U	J. 0214 Of 14 Of 12 21	p-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl		2-Nitro-4-cyanobromobenzeno	o-Bromobenzoic acid	n.C,H,OCH,CH—CH2	5	n-C,H,C(CH3)—CH3

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i.c,H,OCH,CH.—CH2	i-C,H,OCH,CHCH,CHCO,C,H,	50-60	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	524
·c,H,C(CH3)—CH2	;-c,H,c(CH,)CH,CHCO,C,H,	50-60	50-60 NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	525
C <sub>8</sub>	FW H D ODIHO H O "	7.1	NaH	4-C,H,OH	393
n.Cgtt17Df	n-C,H,,CH(CO,C,H,),	80-85	NaOC,H,	Ethanol	282, 743
n.C,H.:.I	n-C,H,,CH(CO,C,H,s),	89	NaOC <sub>2</sub> H	Ethanol	744
n-C,H;.I	$(C_3H_1, \cdot n)_2C(CO_2C_2H_5)_2$	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	745, 615
n·C,H,,CH(CH,)Br	n.C.H.1,CH(CH.)CH(CO.C.H.s).	70-85	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	545, 746
n-C <sub>8</sub> H <sub>13</sub> CH(CH <sub>3</sub> )I	$n \cdot C_{\bullet}H_{13}CH(CH_3)CH(CO_2C_2H_5)_2$	80	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	399, 317
$n$ -C,H $_1$ ,CH(CH $_3$ )CH $_2$ I	$n.\mathrm{C_sH_{11}CH(CH_3)CH_2CH(CO_2C_2H_5)_2}$	83	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	747
::C,H;(CH;),I	1.C,H,(CH2),CH(CO2C,H5),	73	NaOC2H,	Ethanol	138
i-C,H,(CH,),CH(C,H,)Br	$i \cdot C_3H_1(CH_2)_2CH(C_2H_5)CH(CO_2C_2H_5)_2$	43	NaOC,H,	Ethanol	718, 748
$n \cdot C_s H_s CH(C_2 H_s) CH_2 Br$	n·C <sub>4</sub> H,CH(C <sub>2</sub> H,)CH,CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ),	١	NaOC,H,	$n.\mathrm{C_4H_5OH}$	749
$i \cdot C_3H_i(\mathrm{CH}_2)_3\mathrm{CH}(\mathrm{CH}_3)\mathrm{I}$	i.C3H,(CH2)3CH(CH3)CH(CO2C2H5)2	11	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	750
i-C <sub>3</sub> H,CH <sub>2</sub> COC(CH <sub>3</sub> ) <sub>2</sub> Br	i.C.H,CH,COC(CH.),CH,CO.H	1	NaOC,H,	Ethanol	751
$(C_2H_{\mathfrak{s}})_2\mathrm{CBrCO}_2C_2H_{\mathfrak{s}}$	$C_2H_4O_2CC(C_2H_4)_2CH(CO_2C_2H_5)_2$	1	Na	ļ	162
CH,CCI(CO,C,H,),	$(C_2H_6O_2C)_2CHCH(CO_2C_2H_5)_2$	l	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	752
CH.CB.//CO.C.H.A.	$\left\{(C_2H_5O_2C)_2C = C(CO_2C_2H_5)_2\right\}$	1	NaOC2H5	Ethanol	752
0.2021.2021.2021.2021.2021.2021.2021.20	$(\mathrm{CH_3C(CO_2C_2H_5)_2CH(CO_2C_2H_5)_2})$	Low			
$(+,-)\cdot C_2H_5O_2CCHBr$	CHCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>				
CHBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	C2H,O2CCH-C(CO2C2H5)2	80-90	NaOC,H,	Ethanol	175, 485
CH <sub>3</sub> O <sub>2</sub> CCHBr(CH <sub>2</sub> ) <sub>2</sub> - CHBrCO <sub>2</sub> CH <sub>3</sub> (low-melting isomer)	Tetramethyl eyelo- pentane-1,2,2,3-tetracarboxylate*	I	NaOCH,	СН3ОН	753
Note: References 577-1080 are on pp. 322-331.	are on pp. 322–331.				

\* Dimethyl malonate was used in this experiment.
\*\* The halogen was not specified.

Di-L-butyl malonate was used in this experiment.

TABLE I-Continued

Alkylation of Malonic Esters,  $\mathrm{CH}_2(\mathrm{CO}_2\mathrm{R})_2$  (The diethyl ester was used unless otherwise specified.)

Roferenco 753	199, 200				407	663	425	147 730	150, 322
Solvont CH <sub>3</sub> OH	СП,ОН				Ethanol Ethanol	Ethanol	$C_{\mathfrak{g}}\Pi_{\mathfrak{b}}$	Tolueno	Ethanol
Base NaOCH3	$NnOCII_3$				NaOC2Hs NaOC2Hs	NaOC2H3	К	ž Ž	NaOC,115
Yiold, %	89				83 20	20	82	2 Poor	30
Product  Tetramethyl cyclo- pentane-1,2,3,3-tetracarboxylato*	$\begin{array}{cccc} \text{CO}_3\text{CH}_3 & \bullet \\ \text{H}_3\text{C} & & \\ \text{CO}_2\text{CH}_3 & & \\ \text{CH}_3\text{O}_3\text{Cl} & & \\ \end{array}$	0,	ÇO2CH3 *	H,C CO2CH,	Diothyl (y-cyclopentylpropyl)malonato Dicthyl (f-cyclobexylethyl)malonato	Diethyl (\(\beta\)-eyclohexylidene\(\text{cthyl}\)\)malonato	Diethyl [ $eta$ -(1-eyclohexenyl)ethyl]malonute	Diethyl (1-ethyleyelohoxyl)malonato Diethyl (2-ethyl-2-cyclohoxonyl)malonato	Diethyl 2-cyclohexenylmalonate
Alkylating Agent CH <sub>3</sub> O <sub>3</sub> CCHBr(CH <sub>3</sub> )2- CHBrCO <sub>2</sub> CH <sub>3</sub> (high-molting	isomer) (CII <sub>3</sub> O <sub>2</sub> CCHBr) <sub>2</sub> CHCH <sub>3</sub>				$\gamma$ -Cyclopentylpropyl bromido $\theta$ -Cyclohoxylethyl bromido	β-Cyclohoxylidenecthyl	bromido $eta$ -(1-Cyclohoxenyl)othyl	bromide 1.Bromo-1-ethyleyclohoxane 1.Ethyl-1,2-dibromocyclo-	hexano 1,2.Dithiocyanocyclohexano

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;	THU OHOU CHIT	ł	NaOC,H,	Ethanol	427
C,H,(CH <sub>2</sub> ),Cl	Corrections of the control of the co	1	Na	Toluene	208
C,H,CH(CH <sub>3</sub> )Br	Cont. Sout. CH. CH. CO. C. H. J.	65	Na	Toluene	411
C,Hs(CH1)1Br C,Hs(CH1)1Br	$C_{H_s}(CH_2)_2CH^{-5/2}$	80	NaOC <sub>2</sub> H <sub>6</sub>	Ethanol	755, 142, 428, 539, 756, 757
- G ( #10/0 #1 %	C H.O(CH.), CH(CO,C,H.).	68	NaOC,H,	Ethanol	136, 758
$C_{\mathbf{k}}H_{\mathbf{s}}O(\mathrm{CH_2})_2\mathrm{Br}$	C(LT, O(CH, ), 1, C(CO, C, H, ),	1	NaOC,H,	Ethanol	758
$\theta_{\rm e}$ Phenoxyethyl	C4H,0(CH,),CH(CO,C2H,s),	1	NaOC,H,	Ethanol	335
p-toluenesulfonato	o.CH,C,H,CH,CH(CO,H),	0010	NaOC,H6	Ethanol	759, 760
Chloromethyl-	Diethyl [2(and 3)-bromo-5(and 6)-	88	$NaOC_2H_5$	Ethanol	114
a.bromotoluene (mixture)	methylbenzyl]malonate				
OH.C.H.CH.Br	o-CH3C,H,CH2CH(CO2H)2	1	$NaOC_2H_5$	Ethanol	761
OH. C.H. CH. Br	o.CH,C,H,CH,CH(CO,C,H,),	57	Na	Benzene	421
***CH.CH.Br	m.CH,C,H,CH,CH(CO,C,H,),	99	$NaOC_2H_5$	Ethanol	133, 110, 762
m.CH.C.H.CH.CI	CH,C,H,CH,CH(CO,C,H,),	09	NaOC2H5	Toluene	507
2.Methoxy.5-nitrobenzyl	Diethyl (2-methoxy-5-nitrobenzyl)malonate	1	j	1	763
chloride			,		
m-CH <sub>3</sub> OC,H <sub>4</sub> CH <sub>2</sub> Br	$[m\cdot \mathrm{CH_3OC_4H_4CH_2}]_2\mathrm{C(CO_2C_2H_5)}_2$	1	NaOC2H5	Ethanol	764
p-CH <sub>3</sub> OC,H,CH,CI	$p$ -CH $_3$ OC $_4$ H $_4$ CH $_3$ CH(CO $_2$ C $_2$ H $_5)_2$	1	$NaOC_2H_5$	Toluene	511
S HO H SON	(0.NCC,H,CH,CH(CO,C,H,s)),	Good	$NaOC_2H_5$	Ethanol	198, 109
o-MCCentchiol	$(o\text{-NCC}_sH_4\text{CH}_2)_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$	ļ			
C,H,COCH,Br	$C_aH_sCOCH_2CH(CO_2H)_2$	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	765, 106, 766
3.Nitro-4-bromoacetophenone	Dimethyl (2-nitro-4-aeetylphenyl)malonate*	70	Na	Ether	712
3-Nitro-4-methyl-	Dimethyl (2-eyano-4-nitro-5-methyl-	Poor	Na	Ether	712
6-bromobenzonitrilo	phenyl)malonate*				
o-Xylylene dibromido	Diethyl hydrindene-2,2-diearboxylate	75	$NaOC_2H_5$	Ethanol	767, 302, 486
···CsH11OCH2CHCH2	:-C,H,1OCH,CHCH,CHCO,C,E,	20-60	$NaOC_2H_5$	Ethanol	524
Ò	000				

Note: References 577-1080 are on pp. 322-331. \* Dimethyl malonate was used in this experiment.

## TABLE I—Continued

Alexelation of Malonic Esters,  $\mathrm{CH}_2(\mathrm{CO}_2\mathrm{R})_2$  (The diethyl ester was used unless otherwise specified.)

Reference 525	526, 11	<u> </u>	282 317 317 138 686 686	661	317 717 176	725 724
Solvont Ethanol	Ethanol	Ethanel	Ethanol Ethanol Ethanol Ethanol Ethanol	Ethanol	Ethanol Ethanol Ethanol	Ethunol Foluene
Yield, % Base 50-60 NaOC,H <sub>L</sub>	NaOC2H5	NaOC2H5	NaOC,H, NaOC,H, NaOC,H, NaOC,H, NaOC,H,	NaOC.H.	NaOC2H, NaOC2H, NaOC2H,	NnOC <sub>1</sub> H <sub>5</sub> Nn
Yield, % % 50-60	20	46	80-85 90 78 65 80	81 50	50 83	40
Product 7.C3H1,C(CH3)CH2CHCO2C2H5	C <sub>2</sub> H <sub>3</sub> CHCH <sub>2</sub> CH <sub>2</sub>	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	n.C,H;CH(CO,C,H,); n.C,H;CH(CH,)CH(CO,C,H,); n.C,H;CH(CH,)(CH,);CH(CO,C,H,); i.C,H,(CH,),CH(CO,C,H,); i.C,H,(CH,),CH(CO,C,H,); n.C,H,CH,)(CH,)CH(CO,H);	$\mathrm{CH}_{2}\mathrm{=CH}(\mathrm{CH}_{2}),\mathrm{CH}(\mathrm{CO}_{2}\mathrm{C}_{2}\mathrm{H}_{3})_{2}\\ \mathrm{C}_{2}\mathrm{H}_{3}\mathrm{CH}\mathrm{=CH}(\mathrm{CH}_{2})_{2}\mathrm{CH}\mathrm{=CH}.$	$CH_2CH(CO_2C_2H_3)_2$ $C_2H_3CH=C(CH_3)(CH_2)_1CH(CO_2C_2H_2)_2$ $C_2H_3O_2C(CH_2)_1CH(CO_2C_2H_3)_2$ Tetranghyl evelobutene-1,2,2,3.	tetracarboxylato Liethyl (ô-cyclopentylbutyl)mulomato Diethyl (ô-cyclopentylbutyl)mulomato
Alkylating Agent $i \cdot C(H_1) - C(H_2)$	C,H,CH—CH,	p.O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CH—CH <sub>2</sub>	O <sub>p</sub> n.C <sub>p</sub> H <sub>1</sub> ,Br n.C <sub>p</sub> H <sub>1</sub> ,CH(CH <sub>3</sub> )I n.C <sub>p</sub> H <sub>1</sub> ,CH(CH <sub>3</sub> )(CH <sub>2</sub> ),Br i.C <sub>p</sub> H <sub>1</sub> (CH <sub>2</sub> ) <sub>0</sub> I i.C <sub>p</sub> H <sub>1</sub> (CH <sub>2</sub> ),CH(CH <sub>3</sub> )Br n.C <sub>p</sub> H <sub>1</sub> ,CH(CH <sub>2</sub> ),CH(CH <sub>3</sub> )Br	$(c_2\mathbf{H}_2)\mathrm{CH}_2\mathbf{Br}$ $\mathrm{CH}_2\mathbf{H}_2\mathrm{Br}$ $\mathrm{CH}_2\mathrm{CH}(\mathrm{CH}_2)_3$ .	CH=CHCH <sub>2</sub> Cl C <sub>2</sub> H <sub>5</sub> CH=C(CH <sub>3</sub> )(CH <sub>3</sub> ) <sub>4</sub> Br Br(CH <sub>2</sub> ) <sub>5</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> -NaI G T O CHUB <sub>2</sub> -CH CHB <sub>3</sub>	Cartiful Cartiful Cartiful Cartiful Co. Cartiful Co. Cyclopentylbutyl bromide 6. Cyclopentylbutyl bromide

177	704 424	768, 429, 769, 770	771	909	772-774	775, 698, 776, 777	432	18	517	760	412	407	778, 760	779, 738	404	712	780	56	781	524	
ouonjo.I.	Ethanol C <sub>6</sub> H <sub>6</sub>	Ethanol	l	Ethunol	Ethanol	Ethanol	Ethanol	Ethonol	Ethanol	l	Toluono	Ethanol	Xylene	Ethanol	Ethunol	Ethor	Ethanol	Ethanol	Ethanol	Ethanol	
Na	NaOC <sub>2</sub> H <sub>5</sub> K	$NaOC_2H_5$	1	$NnOC_2H_\delta$	$NnOC_2H_{\delta}$	$ m NaOC_2H_5$	$N_0OC_2H_5$	$NaOC_2H_5$	$NnOC_2H_\delta$	I	K	NaOC <sub>2</sub> H <sub>6</sub>	$N_{th}$	$NnOC_2H_{\delta}$	NaOC <sub>2</sub> H <sub>5</sub>	Na	NaOC <sub>2</sub> H <sub>5</sub>	$Mg(OC_3H_5)_3$	NaOC <sub>2</sub> H <sub>5</sub>	$NnOC_2H_\delta$	
1	53 71	78	l	1	20	84	09	51	85	Good	82-85	78	49	30	77	I	99	l	l	20-00	
Diethyl [8-(2-cyclopontenyl)butyl]malonato	Diethyl (y-cyclohoxylpropyl)malonato Diethyl [f-(2-methyl-1-cyclo-	hexenyl)ethyl jmaionato $\mathrm{C}_{_{0}}\mathrm{H}_{_{3}}(\mathrm{CH}_{_{2}})_{_{3}}\mathrm{CH}(\mathrm{CO}_{_{2}}\mathrm{C}_{_{2}}\mathrm{H}_{_{3}})_{_{2}}$	C,H,(CH,),CH(CO,C,H,),	C,H,CH,O(CH,),],C(CO,C,Hs),	C,H,O(CH3),CH(CO,C,H3),	C,H,O(CH,),CH(CO,C,H,),	C,H,CH,CH(CH,)CH(CO,C,H,),	$C_AH_ACH=CHCH_ACH(CO_AC_AH_A)_2$	m.CH,C,H,(CH,),CH(CO,C,H,),	p·CH <sub>3</sub> C <sub>4</sub> H <sub>4</sub> (CH <sub>2</sub> ) <sub>2</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	m.CH,OC,H,(CH,),CH(CO,C,H,),	Diethyl (2-brome-5-ethylbenzyl)malonato	Diethyl (2,4-dimethylbenzyl)malonato	Diethyl (3,5-dimethylbenzyl)malonate	Diethyl (2-methyl-5-mothoxybenzyl). malonato	Diethyl (2-acetyl-4-nitro-5-mothyl-	$P_{\rm rec}$ $(p$ -carbomethoxybenzyl) malonato	$(C_a H_s C H_s C O C H_s)_s C (C O_s C_s H_s)_s$	Dietly (2-chloro-3-indenonyl)malonato	$^{n\cdot C_dH_{13}OCH_2CHCH_2CHCO_2C_2H_5}$	000
3.(2.Cyclopentenyl)butyl	bromido y.Cycloloxylpropyl bromido \(\hbar{\eta}\).Cyclolylpropyl bromido \(\hat{\eta}\).Cyclolyl-I.cycloloxenyl).	cthyl bromide C <sub>e</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>3</sub> Br	C.H.(CH.),	Carraction CH. Circ. Oct. Oct. Circ. Circ. Oct. Circ. Oct. Circ. Circ. Oct. Circ. Circ. Oct. Circ. Circ. Circ. Circ. Circ. Oct. Circ. C	C.11.0/CH.),Cl	C <sub>6</sub> II <sub>5</sub> O(CH <sub>2</sub> ) <sub>3</sub> Br	G.H.CH.CH(CH.)Br.KI	C.II.CH=CHCH,Cl	m.CII,CIII,(CH.),Br	p.CH,C,H,(CH,),Br	m.CH,OC,H,(CH,),Br	2-Bromo-5-ethylbenzyl chloride	2,4.Dimothylbenzyl chlorido	3,5.Dimethylbenzyl bromide	2-Methyl-5-methoxybenzyl elloride	2-Chloro-5-nitro-4-	Mothyl p-chloromothyl-	C,TI,CH1COCH1CI	S.A. Dichloroindenone	0	

Note: References 577-1080 are on pp. 322-331,

#### TABLE I-Continued

Alkylation of Malonic Estens,  $\mathrm{CH}_2(\mathrm{CO}_2\mathrm{R})_2$  (The diothyl ester was used unless otherwise specified.)

Reference 525	\$25.	523	782	70, 282, 289 684 784 784 141 743	18, 282, 785 19 19 786	787 787 788
Solvent Ethanol	Ethanol	Ethanol	C,II,	Ethanol Ethanol — Ethanol	Ethanol Ethanol Ethanol C <sub>e</sub> H <sub>6</sub>	Ethanol Ethanol Ethanol
Baso NaOC <sub>2</sub> H <sub>2</sub>	NaOC,H,	50-60 NaOC <sub>2</sub> H <sub>5</sub>	Na	NaOC;H <sub>5</sub> NaOC;H <sub>5</sub> NaOC;H <sub>5</sub>	NaOC,H; NaOC,H; NaOC,H; Na	NaOC,H; NaOC,H; NaOC,Hs
Yield, % % 50-60	20-60	20-60	2. 73	2 8 8 8 6 2 8 8 8 6	4. 00. 00. 00. 00. 00. 00. 00. 00. 00. 0	50 10 33
(The diothyr caret ma)  Product  n.C <sub>6</sub> H <sub>13</sub> C(CH <sub>3</sub> )CH <sub>2</sub> CHCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	0 $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$	$\begin{matrix} \begin{matrix} 0 & & CO \\ C_s H_s C(CH_s) CH_s CHCO_2 C_2 H_s \end{matrix}$	6———CO Diethyl (3-thianaphthenemethyl)malonato	n:C <sub>10</sub> H <sub>21</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ); n-C <sub>10</sub> H <sub>21</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ); n-C <sub>3</sub> H <sub>1</sub> ;CH(CH <sub>3</sub> )CH(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> );†† n-C <sub>2</sub> H <sub>1</sub> CH(C <sub>1</sub> H <sub>2</sub> ·n)CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ); i.C <sub>3</sub> H <sub>7</sub> (CH <sub>3</sub> )CH(CH <sub>3</sub> )(CH <sub>3</sub> );CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> );	Diethyl geranylmalonato Diethyl geranylmalonate Diethyl geranylmalonato i.C,H,(CH,),CH(CH,)OOOH,CH(CO,C,H,);	C,H,O,C(CH,),CH(CO,C,H,)CH(CO,C,H,), {C,H,O,C(CH,),CH(CO,C,H,)},C(CO,C,U,), Br(CH,)C(H(CO,C,H,)),
Alkylating Agent ".C.H.,CiCH.)—CH.	C,H,OCH,CH—CH2	$C_{g}H_{\delta}C(CH_{3})$ — $CH_{2}$	3. Chloromethylthianaphtheno	$\mathcal{O}_{10}$ $n.C_{10}H_{21}$ Br·KI $n.C_{10}H_{21}I$ $n.C_{8}H_{17}$ cH(CH <sub>3</sub> )Br $n.C_{8}H_{17}$ CH(CH <sub>3</sub> )Br $n.C_{8}H_{17}$ CH(C <sub>4</sub> H <sub>2</sub> $n$ )I	(CH3,273 (CH3,273 Geranyl chlorido Geranyl bromide Linalyl bromide	COCHAB: C2H,O2C(CH2),CHBrCO2C,H, C2H,O2C(CH2),CHBrCO2C,H, Br(CH2),0Br

TABLE I—Continued

Alkylation of Malonic Estens,  ${\rm CH_2(CO_2R)_2}$  (The diothyl ester was used unless otherwise specified.)

Solvont Roforonco Ethanol 799	сн <sub>3</sub> ОН 800	Ethanol 801	Ethanol 524	Ethanol 524	Ethanol 524	Ethanol 524	Ethanol 524
$\rm Basc \\ NaOC_2H_b$	$N_{R}OCH_{3}$	NaOC2H6	$ m NaOC_2H_{8}$	$NaOC_2H_5$	${ m NaOC_2H_5}$	NaOC <sub>2</sub> H <sub>6</sub>	NaOC2Hs
79 79	1	į	50-60	20-60	50-80	20-80	50-60
Preduct Diothyl (3-indenylmethyl)malonate CHCO <sub>2</sub> CH <sub>3</sub> *	H,C,CH—C(CO,CH,),	O CH(CO <sub>2</sub> C <sub>2</sub> H <sub>6</sub> );	$\begin{array}{c c} & & & & \\ & & & & \\ & & & & \\ & & & & $	C,H,CH,OCH,CHCO,C,H,	OCO O-CH3C,H,OCH2,CHCH2CH2C4L6 	O0 o.CH3OC,H4OCH2CHC3	m.CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> OCH <sub>2</sub> CHCH <sub>2</sub> CHCO <sub>2</sub> C <sub>2</sub> H <sub>6</sub>
Alkylating Agent 3-Bromomethylindeno	$C_{\bullet}II_{5}CHBrCHBrCO_{2}CH_{5}$	Dibromothymoquinene	n.C,H,OCH,CH——CH,	C,H,CH2OCH2CH—CH2	O. O.CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> OCH <sub>2</sub> CHCH <sub>2</sub>	°CH3OC4H4OCH2CH—CH2	m·CH <sub>3</sub> C <sub>4</sub> H <sub>1</sub> OCH <sub>2</sub> CH—CH <sub>2</sub>

#### TABLE I-Continued

(The diethyl ester was used unless otherwise specified.) ALKYLATION OF MALONIC ESTERS, CH2(CO2R)2

Alkylating Agent 3,4-Dibromo-\theta- naphthoquinone	Product Diethyl [(1) -bromo- <i>f</i> i-naphtho- quinone]malonato	Yield, %	Base NaOC <sub>2</sub> H <sub>5</sub>	Solvent Ethanol	Referenco 781
$\mathcal{C}_{11}$ $n.C_{11}H_{23}\mathrm{Br}$ $n.C_{41}_{14}\mathrm{CH}(CH_{3})\mathrm{Br}.\mathrm{NaI}$ $CH_{2}=CH(CH_{1})_{4}\mathrm{Cl}.\mathrm{KI}$ $n.C_{4}H_{3}\mathrm{CH}(CH_{1})_{4}\mathrm{Cl}.\mathrm{KI}$	n-C <sub>11</sub> H <sub>23</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>3</sub> H <sub>15</sub> CH(CH <sub>3</sub> )CH(CO <sub>3</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> CH <sub>3</sub> =CH(CH <sub>1</sub> )CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>1</sub> H <sub>2</sub> CH(CH <sub>2</sub> ) <sub>1</sub> CH(CH <sub>3</sub> ) <sub>2</sub>	80-85 70 75 71	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>6</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ethanol Ethanol Ethanol	282, 802 70 804 686
(CH <sub>2</sub> ) <sub>2</sub> CH(CH <sub>3</sub> )Br ε-Cyclohexylpentyl bromide	Ch(Coronalisa Diethyl (e.cyclohexylpentyl)malonate	7.0	NaOC2Hs	Ethanol	704
C,H,O(CH,),Br	C,H,O(CH,),CH(CO,C,H,),		NaOC,Hs NaOC,Hs	Ethanol Ethanol	805 805
n-C <sub>4</sub> H <sub>3</sub> CH(C <sub>6</sub> H <sub>5</sub> )Dr l-C <sub>4</sub> H <sub>3</sub> CH(C <sub>6</sub> H <sub>5</sub> )Br	$i:C_4\Pi_3$ CH( $C_6\Pi_3$ )CH( $CO_2C_2\Pi_3$ ); $i:C_4\Pi_3$ CH( $C_6\Pi_3$ )CH( $CO_2C_2\Pi_3$ );	24	NaOC2H5	Ethanol	908
p.t.C.H,C,H,CH,CI	p-t-C <sub>4</sub> H,C,H,CH <sub>2</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ),	1 \$	NaOC,H,	Ethanol Ethanol	403 404
y-(2-Methyl-5- methoxyphenyl)propyl bromide	Dictnyl [y.{z-meunyl-3-meunoxy- phenyl)propyl]malonato	ĵ.	2000		
$\beta$ -(2,5.Dimethyl-4-methoxyphenyl)ethyl	Diethyl [ $eta$ -(2,5-dimethyl-4-methoxyphenyl)ethyl]malonate	54	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	807
2-Methyl-5-isopropylbenzyl chloride	Diethyl (2-methyl-5-isoproplbenzyl)- malonate	09	Na	C,H,	808, 418, 779
2,3,5,6-Tetramethylbenzyl chloride	Diethyl (2,3,5,6-tetramethylbenzyl)malonate	99	Na	C,H,	808
2,3,5,6-Tetramethylbenzyl chloride	eta.(2,3,5,6-Tetramethylphenyl)propionie acid	72	$\mathrm{NaOC_2H_5}$	Ethanol	010

## TABLE 1-Continued

Alkylation of Malonic Estens,  ${\rm CH}_2({\rm CO}_2{\rm R})_2$  (The dictiyl exter was used unless otherwise specified.)

Mkylating Agent ethylnaphtbalene bene ethylnaphtbalene chynnenethyl- lene ethylnaphthalene bronomethyl-	(1 ne the try to each the the the the the the the the the th	Yield.	Base Na Na Na	Solvent C <sub>4</sub> H <sub>6</sub> C <sub>4</sub> H <sub>6</sub> C <sub>4</sub> H <sub>6</sub> C <sub>4</sub> H <sub>6</sub>	Reference 153 153 153 153
(c'11,9216. 1,187 1,187	(n·C;1,H3,),C(CO,H), n·C;1,H3,C(CH3,)CH(C,H3,)CH4,CH(CO,C;H3), (C,H1,O,C),C(C,H3)(CH2),CH(CO,C;H3,),	80	NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub>	Ethunol Ethanol Ethunol	684 680 814, 656
, <sup>11</sup> , <sub>1</sub> (C'11,2,13r <sub>2</sub> ,43r H <sub>s</sub> (C'11 <sub>2</sub> ),3r	cyclo-C <sub>6</sub> H <sub>11</sub> (CH <sub>4</sub> ) <sub>4</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>3</sub> C <sub>6</sub> H <sub>2</sub> O(CH <sub>2</sub> ) <sub>5</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>5</sub> / p.t.C <sub>1</sub> H <sub>3</sub> CH <sub>4</sub> (CH <sub>2</sub> ) <sub>2</sub> CH(CO <sub>3</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>   p.t.C <sub>1</sub> H <sub>3</sub> CH <sub>4</sub> (CH <sub>2</sub> ) <sub>2</sub> H <sub>3</sub> (CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	50	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> Na	Ethanol Ethanol C <sub>6</sub> H <sub>&amp;</sub>	704 815, 816 321
hyl. I-isopropyl- lkenzene	CH3 (CH3),CH(CO,C,H3),	30	Nn	С,Н,	415
/l-2-methyl-4- ylwnzyl chlorido	CH(CH <sub>3</sub> ) <sub>3</sub> Diethyl (2-methyl-4-methoxy-5- i-copropylbenzyl)mulonate	63	NaOC <sub>2</sub> H <sub>6</sub>	Ethanol	404

## TABLE I-Continued

Alkylation of Malonic Esters,  ${\rm CH_2(CO_2R)_2}$  (The diethyl ester was used unless otherwise specified.)

0000000	Reference	827, 414	827	405	321	413	828	516, 829 830 738	712 520	818	831
	Solvont	Ethanol	Ethanol	Ethanol	Ethanol	Tolueno	Ethanol	Ethanol	Ether Ethanol	$_{ m C,H_6}$	Tolueno
	Baso	NaOC2H5	$NaOC_2H_5$	NaOC2H5	$NaOC_2H_5$	Na	NaOC2H3	NaOC <sub>2</sub> H <sub>5</sub>	Nu NaOC <sub>2</sub> H <sub>5</sub>	Na	አ
Viold	0,0	% 80 80	55	19	1	61	1	49 80 65	65	80	37
		Product  Product  Product  Product	Diethy! [\(\beta\): \(\frac{1}{2}\)-methy! \(\frac{1}{2}\)-\(\frac{1}\)-\(\frac{1}\)-\(\frac{1}2\)-\(\frac{1}\)-\(\frac{1}\)-\(\frac{1}2\)-\(\	Diethy! [p-(2-methexy-2-mas); phenyl)ethyl]malenate Diethy! (9-4-dimethyl-5-t-butylbenzyl)-	Declay (ST) malonato $i \cdot H_2 C_3                                  $	CH3O\_\CH3\\CH3\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	CH <sub>3</sub> O CH <sub>3</sub>	Diethyllmalonato Diethyl benzhydrylmalonato o-C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub> CH <sub>5</sub>		Diothyl [2. (7.mothoxy-2.naphthyl)othyl]-	malonato malonato malonate malonate
		Alkylating Agent	$\beta$ .(2-Methyl-4-t-butylphenyl)-othyl bromido	$\beta$ -(2-Mothoxy-5- $t$ -butylphenyl)othyl bromido	2,4.Dinethyl.5.4.butylbenzyl chloride	CH <sub>3</sub> O CH <sub>3</sub>	$i.H_1C_3$ $CH_3O$ $CH_3$	1.Benzoyl-4.bromo- methylpiporidino Benzlıydryl bromide o-C <sub>0</sub> H <sub>5</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	p.C.H.CH.CH.CI 3.Nitro-4.bromobenzophenone	β.(5-Methoxy-1-naphthyt)· ethyl bromido	$\beta$ -(7-Mothoxy-z-nupheny); othyl bromido $\beta$ -(6-Mothoxy-1-naphthyl); othyl bromido

C(CH <sub>3</sub> ) <sub>2</sub> Cl	C(CH <sub>3</sub> ) <sub>2</sub> CH(CO <sub>2</sub> H) <sub>2</sub>	15	Na	Ether	832
I-Chloromethyl-2-ethyl-	Diethyl (2.ethyl-1-naphthylmethyl)malonato	}	1	I	821
naphthaleno 1-Chloromethyl-2,3-	Dicthyl (2,3-dimethyl-1-naphthylmethyl)-	1	l	1	821
dinethylnaphthalone 1-Chloromethyl-3,4	malonate Dicthyl (3,4-dimethyl-1-naphthylmethyl)-	1	I	ı	821
dimethylnaphthalene 9-Bromofluorene	malonate Fluorenyl-9-acetie acid	80	$NaOC_2H_5$	Ethanol	833, 516
C11-C18	.C. HCH/CO.H.).	96	e Z	None	684
$n.C_1H_9CH(C_2H_3)(CH_2)_2$ .	$n \cdot C_1 + r_2 = C_2 \cdot C_3 \cdot C_4 \cdot C_4 \cdot C_4 \cdot C_4 \cdot C_5 \cdot $	31	NaOC,H,	Ethanol	989
CH(C,H,·,1)Br n.C,H,CH(C,H,)(CH <sub>2</sub> ) <sub>3</sub> Br	$^{\mathrm{CH}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_3)_2}_{n\cdot\mathrm{C}_1\mathrm{H}_2\mathrm{CH}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_3)_2}$	99	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	805
p·C <sub>6</sub> H <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	$(p\cdot C_0H_5COC_0H_4CH_2)_2C(CO_2C_2H_5)_2$	76	NaOC2H3	$c_{ m eH_6}$	834
CH <sub>2</sub> Br	CH <sub>2</sub>				
CH <sub>2</sub> Br	C(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> ) <sub>2</sub>	1	NaOC <sub>2</sub> H 5	Ethanol	492
$\iota$ ·H <sub>5</sub> C <sub>4</sub> (CH <sub>2</sub> ) <sub>3</sub> Br CH <sub>3</sub> O (CH <sub>3</sub> )	$\iota_{-H_3C_4}$ $(\mathrm{CH}_z)_2\mathrm{CH}(\mathrm{CO}_z\mathrm{C}_z\mathrm{H}_z)_2$ $\mathrm{CH}_z\mathrm{O}_z\mathrm{C}_z\mathrm{H}_z$	}	1	1	414
$p\cdot\mathrm{CH}_3\mathrm{DC}_6\mathrm{H}_4\mathrm{SO}_2\mathrm{C}_6\mathrm{H}_4\mathrm{CH}_2\mathrm{Br}\cdot p$ 1-Chloromethyl-4- isopropylnaphthalenc	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>7</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyl (4-isopropyl-1- naphthylmethyl)malona <i>te</i>	40	$_{\rm NaOC_2H_5}$	C <sub>6</sub> H <sub>6</sub> Ethanol	245 515

Note: References 577-1080 are on pp. 322-331.

# TABLE I—Continued

Alkylation of Malonic Esters,  ${\rm CH_2(CO_2R)_2}$  (The diethyl ester was used unless otherwise specified.)

		Yield.			0 - 0
Allcylating	Product	è <sup>0</sup>	Ваѕо	Solvent	Kolerence
	<b>&gt;</b>			forester	833
	CH.O.CHICO.	i	NaOC2H5	Femilia	656
(CH <sub>2</sub> ) <sub>2</sub> Br	(CH.O.C),C(C,H,1,-n)(CH1,1,CH(CO,CH1,1,*	İ	Nn	None	
$Br(CH_2)_2C(C_2H_1s^2n)^2$	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2		NoOC II.	Ethanol	836
(CO3CH2)3	Diothyl (3,7,11-trimethyl-2-dodecenyl)-	i	ANO C2113		
3,7,11. Iffinedity: "	malonato	ď	NoOC.1f.	Ethnuol	837
Fornesyl bromide	Diethyl farnesylmalonate	?		1	929
Br(CH2),C(C,H11.n).	(C2H3O2C)2C(C3H11-n)(CH2)2CH(CU2C2H3)2				
$(CO_3C_2H_6)_2$					
	C(CO2C2H5)2			•	100
•	or C/CO C H.). and	!	NaOC, II,	Ethanol	101
$(C_2H_5O_2C)_2CBrCH_2$ .					3
CBr(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	(C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C) <sub>2</sub> CITOTI (CO <sub>2</sub> C <sub>2</sub> C <sub>2</sub> T <sub>2</sub> S) <sub>2</sub>	56	NnOC, H5	Ethanol	808
$n_{\cdot}C_{\bullet}H_{\cdot},CH(C_{\bullet}H_{\circ})C!$	n-C, H, CH(C, H, S) CH(CO, O2, 1, S)?	1	ļ	i	821
1.Chloromethyl-2-t-	Diethyl (2.t-butyl-1-naphthyl-				
butylnaphthalene	methyl)malonato	69	NaOCII,	Xyleno	838
$\beta$ -(5-Isopropyl-1-naphthyl)-	Diethyl [p-(5-180propyr-1-mapmay.por.g-)				
othyl bromido	malonaco				

839	679, 840, 841	842	843	844	845, 846	847	261		802	805	400	281	281	848	46, 45, 684	849	678	040	000	000	040
C <sub>6</sub> H <sub>6</sub> -ethanol	Ethanol	Ethanol	Ethanol	$n$ - $C_4$ $H_9$ $O$ $H$	Ethanol	Ethanol	Ethanol		Ethanol	Ethanol	$C_6H_6$	Ethanol	Ethanol	$C_nH_n$	$n.C_4H_9OH$	. 1	ı	Ethanol	Ethanol	C.H.	99)
N	$NaOC_2H_5$	$NaOC_2H_5$	$NaOC_2H_5$	$NaOC_4H_9-n$	$NaOC_2H_5$	$NaOC_2H_5$	$NaOC_2H_5$		$NaOC_2H_5$	$NaOC_2H_5$	Na	NaOC <sub>2</sub> H5	$NaOC_2H_5$	Na	NaOC,H9-n	1	ı	NaOC,H,	NaOC,H,	Na Na	
42	94	40	i	40-50	> 29	59	ł	č	19	67	92	20	06	92	100	53	09	I	61	>93	
CH, CH, CO2H	$n\cdot c_1$ $_4H_{33}$ $\mathrm{CH}(\mathrm{CO_2}c_2H_5)_2$	n-C <sub>16</sub> H <sub>33</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> and (n-C <sub>16</sub> H <sub>33</sub> ) <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	$n \cdot C_a H_{13} CH = CH(CH_2)_s CH(CO_2 C_2 H_5)_2$	$C_2H_5CH$ — $CH(CH_2)_{12}CH(CO_2C_2H_5)_2$	$n \cdot C_1H_{11}C = CCH_2C = C(CH_2)_6CH(CO_2C_2H_5)_2$	Diethyl hydnoearpylmalonato	$(C_2H_5O_2C)_2\mathrm{CHCH}(CO_2C_2H_6)_2$ and $\mathrm{CH}_3\mathrm{C}(CO_2C_2H_5)_2$	CH2—C(CO2C2H3)2	11.Cot.110.C11(Cot.5/CH(CC2C2Hs/2	n-C,H,UH(C,H,S)(CH,S),CH(CO,C,H,S),	n-C17H35CH(CO2C2H5)2	"-C15H31CH(CH3)CH(CO2C2H5)2	"CISH 31CH(CH3)CH(CO2C2H3)2	Diethyl (3-pyrenylmothyl)malonato	$n \cdot c_{18} H_3 \cdot \text{CH}(\text{CO}_2 \text{C}_2 \text{H}_5)_2$	Diethyl oleyimalonato	Diethyl oleylmalonato	Diethyl ehaulmoogrylmalonato	"-C,H,CH(C,H,)(CH,),CH(CO,C,H,),	Diethyl [ $\alpha$ -(3-pyrenyl)ethyl]malonate	aro on pp. 322-331.
CH <sub>3</sub> Br	11.C14H33Br	n.C141133I	n.C,H13CII=CII(CH2),Br	C2H,CH=CH(CH2)12Br	".C,II,IC=CCH2C=C(CH2),I	Hydnocarpyl bromide	(C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> C) <sub>3</sub> CBr(CH <sub>3</sub> ) <sub>2</sub> . CBr(CO <sub>3</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	n.G.11CH(G.H.)C!	10/2118/0118/118/11 11/11 11 11/11 11 11/11 11 11/11 11	".C'11 T T T T T T T T T T T T T T T T T T	. C II OHIOH M	"Clst131Cr1(Ct13)Bf	"Chlomusticularian	a.C. 1f r	Olari bramida	Olevi temilate	Chambras and	Circumogryi bromide	"Canson (Cans) (CH2), CI	a-(a-monucony)pyrene	Note: References 577-1080 are on pp. 322-331

Note: References 577-1080 are on pp. 322-331.  $\bullet$  Dimethyl malenate was used in this experiment.

## TABLE I-Continued

Alkylation of Malonic Esters,  $\mathrm{CH}_2(\mathrm{CO}_2\mathrm{R})_2$  (The diethyl ester was used unless otherwise specified.)

Reference	805 hanol 218 56 851 805 829	829	820	829	852		
Solvent	Ethanol Ether-ethanol Ether Ether Ethanol	Ethanol	Ethanol	Ethanol	1		
Base	NaOC <sub>2</sub> H <sub>5</sub> Mg(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Ng(OC <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> NaOC <sub>2</sub> H <sub>5</sub>	$\mathrm{Mg}(\mathrm{OC_2H_5})_2$	${ m Mg(OC_2H_5)_2}$	${ m Mg}({ m OC_2H_5})_2$			
x lolu, % %	72 84 86 142 69	7.7	85	1	1		
Product	n.C,H <sub>19</sub> CH(C,H <sub>3</sub> )(CH <sub>2</sub> ),CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ); Dicthyl (dimesitylmethyl)malonato (C <sub>4</sub> H <sub>3</sub> ),CCH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ); (C <sub>4</sub> H <sub>3</sub> ),CCH(CO <sub>2</sub> C,H <sub>3</sub> ); n.C,H <sub>1</sub> CH(C <sub>4</sub> H <sub>3</sub> )(CH <sub>2</sub> C,H <sub>3</sub> ); Dicthyl (diphenyl-o-tolylmethyl)malonato	Diethyl (diphenyl- $p$ -tolylmethyl)malonato	Diethył (diphenyl-o-methoxyphenylmethyl)-	malonato Diethyl (diphenyl-p-methoxyphenylmethyl)·	malonato CH <sub>3</sub>	$\begin{array}{c} \text{CO}_{1}\text{C}_{1}\text{H}_{5}\\ \text{CH}_{2}\text{CH}(\text{CO}_{5}\text{C}_{2}\text{H}_{5})_{1} \end{array}$	CH <sub>3</sub> O <sub>C</sub> H <sub>3</sub> O
Alkylating Agent	C <sub>1,1</sub> -C <sub>1,1</sub> n.C <sub>1</sub> II <sub>1</sub> ,CH(C <sub>4</sub> II <sub>4</sub> )(CH <sub>2</sub> ),Br Dimesitylehloromothano (C <sub>4</sub> II <sub>4</sub> ),5CCl (C <sub>4</sub> II <sub>4</sub> ),2CBr n.C <sub>4</sub> II <sub>4</sub> ,2CBr Diphenyl-a-tolylmethyl	bromide Diphenyl-p-tolylmethyl	bromido Diphenyl-o-methoxyphenyl-	methyl bromide Diphenyl.p.methoxy.	phenylmethyl bromide CH3	CO,C,H,	Си, о

$n$ -C, $H_{i,I}$	$n$ - $\mathrm{C_{22}H_{45}CH(CO_{2}C_{2}H_{5})_{2}}$	92	$\mathrm{NaOC_2H_5}$	Ethanol	802, 134, 684
n.C.H.,CH==CH(CH,),Br	$n \cdot C_s H_1$ , $CH = CH(CH_2)_{12} CH(CO_2 C_2 H_5)_2$	78	$NaOC_2H_5$	Ethanol	853
".C.H.,CH(C.H.)(CH,),Cl	n.C.H.,CH(C,H,)(CH,),CH(CO,C,H,),	57	$NaOC_2H_5$	Ethanol	805
".C.HCH(C.H.)(CH,),Br	n.C.H.,CH(C.H.)(CH.),CH(CO,C.H.),	73	$NaOC_2H_5$	Ethanol	805
:-C.H.(CIL),.I	.C,H,(CH,),,CH(CO,C,H,),	1	NaOC2H3	Ethanol	854
n.C.,H.,CH(C,H.,-n)(CH.),I	$n \cdot C, H, CH(C, H, -n)(CH_2)$ $CH(CO_2C_2H_3)$	16	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	20
$n$ -C, $H_1$ , $CH(CH_3)CH_2CH=$	n.C,H1,GH(CH3)CH2CH=C(CH3)(CH2)8-	13	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	855
$C(CH_3)(CH_2)_aCH(CH_3)I$	CH(CH <sub>3</sub> )CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>				
$n \cdot C_{\mathfrak{g}}H_{1,\mathfrak{g}}CH = C(CH_3)(CH_2)_{\mathfrak{g}}.$ $CH(CH_3)I$	$n.C_9H_{19}CH=C(CH_3)(CH_2)_0CH(CH_3)CH$ . $(CO_2C_2H_2)_a$	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	856
Diphenyl-a-naphthylmethyl	Diethyl (diphenyl-x-naplıtlıylmethyl)-	38	${ m Mg}({ m OC}_2{ m H}_5)_2$	Ethanol	829
bromide	malonate				
n-C,H1,CH(CH3)(CH2)2-	$n \cdot C_9 H_{1,0} CH(CH_3)(CH_2)_2 CH(CH_3)(CH_2)_{1,0}$	1	$NaOC_2H_5$	Ethanol	317
$CH(CH_3)(CH_2)_{10}Br$	$CH(CO_2C_2H_5)_2$				
$n \cdot C_3H, CH = C(CH_3)(CH_2)_1$ .	$n \cdot C_3H$ , $CH = C(CH_3)(CH_2)$ , $CH = C(CH_3)(CH_2)$ ,	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	856
$CII = C(CH_3)(CH_3)_4CH(CH_3)I$	CH(CH <sub>3</sub> )CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>		•		
Diphenyl-4-biphenylylmethyl bromide	Diethyl (diphenyl-4-biphenylylmethyl)malonato	89	${ m Mg(OC_2H_5)_2}$	Ethanol	829
3eta-Cholestanyl	Diethyl 3x-eholestanylmalonate	1	Na	Toluene	10
p-toluenesulfonato					
3\beta-Cholesteryl	Diethyl 3-cholesterylmalonate and	١	Na	Xylene	21, 22
p-toluenesullonato 3 $eta$ -Cholestervl	diethyl 3,5-cyclo-6-cholestanylmalonate		ļ		
p-toluenesulfonato	orenyi σχ. and σρ.cnoiesteryinalonateγ†	1	Na	Toluene	10

Note: References 577–1080 are on pp. 322–331. †† The ratio of the  $\beta$ -isomer to the  $\alpha$ -isomer was about 9 to 1,

#### TABLE II

ALKYLATION OF CHLORO., NITRO., AMINO. AND ACYLAMINO-MALONIC ESTERS, XCH(CO2R),

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	TILL GENERAL COURT WAS USED TOTAL TOTAL	•			
Alleylating		Yield,	Baso	Solvent	Refer-
Agent	Product	%			enee
o cook	C. H.O.C), C)=C(CO.C.H.),	09>	$NaOC_2H_5$	Ethanol	857
SHO	(C.H.O.C), CHCH(CO.C.H.)	١	NaOC2H5	Ethanol	231
CHR	(C.H.O.CHCHCHCO,C.H.),	ı	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	231
CHI	(C.H.O.C), CHCH(CO.C.H.),	l	NaOC, Hs	Ethanol	231
4.Imidazovlmethyl	Diethyl [4-(or 5-)-imidazoylmethyl]-	09	$NaOC_2H_5$	Ethanol	209
chleride hydrechloride	chloromalonate				
C.H.CH,CI	$C_sH_sCH_sCCI(CO_sC_sH_s)_s$	26	$NaOC_2H_5$	Ethanol	508
o.Xvlvlene dibromide	0.C,H,CH,CCI(CO,C,H,),1,	l	$NnOC_2H_5$	Ethanol-ether	228
m-Xylylene dibromide	$m \cdot C_A H_A \Gamma C H_A C C \Gamma (CO_A C_A H_A)_A J_A$	100	$NaOC_2H_s$	Ethanol-ether	220
p-Xylylene dibromide	$p.C_{\rm s}H_{\rm s}[{ m CH_sCCl}({ m CO_2C_2H_s})_2]_2$	ł	$NaOC_2H_5$	Ethanol-ether	550
p.Carbethoxybenzyl	Diethyl (p-carbethoxybenzyl).	Fair	ĺ	Į	230
bromide	chloromalonato				
CH,=CHCH,Br	$CH_2 = CHCH_2C(NO_2)(CO_2C_2H_5)_2$	34	$KOC_2H_s$	Ethanol	183
CH,CH=CHCH,Cl	$CH_1CH = CHCH_2C(NO_2)(CO_2C_2H_5)_2$	25	$KOC_2H_5$	Ethanol	183
CH,Br	CH,C(NH,)(CO,C,H,),	20	$NaOC_2H_5$	Ethanol	828
$CH_3I$	CH,C(NH,)(CO,C,H,),	20	NaOC2H5	Ethanol	858
$(CH_3)_sSO_s$	CH <sub>3</sub> C(NH <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	20	NaOC2H5	Ethanol	858
$CH_2$ = $CHCH_2B_r$	$CH_2$ = $CHCH_2C(NH_2)(CO_2C_2H_5)_2$	l	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	859
	$\mathrm{CH_2-CH_2}$				
$\mathrm{Br}(\mathrm{CH}_2)_3\mathrm{Br}$	CH <sub>2</sub> CHCO <sub>2</sub> H	25	$NaOC_2H_{\delta}$	Ethanol	434
	H				
$i\text{-}\mathbb{C}_4\mathbb{H}_9\mathrm{I}$	$i \cdot \mathrm{C}_{\mathtt{i}}\mathrm{H}_{\mathtt{o}}\mathrm{C}(\mathrm{NH}_{\mathtt{z}})(\mathrm{CO}_{\mathtt{z}}\mathrm{C}_{\mathtt{z}}\mathrm{H}_{\mathtt{s}})_{\mathtt{z}}$	55	Na	$i.C_4H_5OCH_3$	859

NO,

$\begin{array}{cccccccccccccccccccccccccccccccccccc$	HCONH	C,H,CH,Br i.C,H,Br	C,H,CH,C(NH2)(CO,C,H,8)2 i-C,H,C(NHCHO)(CO,C,H,8)2	60 50	Na NaH	Ether (CH <sub>3</sub> ) <sub>2</sub> NCHO	859 246
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		CH <sub>2</sub> —CHCH <sub>2</sub> Cl	CH <sub>2</sub> =CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	69	$N_{a}H$	Toluono	860
$cis. \text{CICH} = \text{CHCH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ trans. \text{CICH} = \text{CHCH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ trans. \text{CICH} = \text{CHCH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ \text{S3}  \text{NaH}  \text{Toluene} \\ \text{CH}_2 = \text{CSICH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ \text{CH}_3 = \text{CSICH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ \text{CH}_4 = \text{CBrCH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ \text{BrCH} = \text{CHCH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ \text{BrCH}_2(\text{CHCH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ \text{BrCH}_2(\text{CHCH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ \text{BrCH}_2(\text{C(NHCHO)}(\text{CO}_2 C_2 H_s)_2) \\ \text{BrCH}_2(C($		CH(CH,),Br	CH <sub>2</sub> =CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> ); Cl(CH <sub>2</sub> ),C(NHCHO)(CO <sub>2</sub> C <sub>3</sub> H <sub>2</sub> ),	1 1	1 1	1 1	801 436
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		cis-ClCH=CHCH,Cl	cis-CiCH=CHCH2C(NHCHO)(CO,C,H5),	84	NaH	Tolueno	860
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		trans-ClCH=CHCH2Cl	trans-CICH=CHCH2C(NHCHO)(CO2C2H5)2	98	NaH	Toluene	860
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		CH2-CCICH2CI	CH2=CCICH2C(NHCHO)(CO2C2H5)2	83	NaH	Toluene	246
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		CH2=CBrCH2Br	CH2=CBrCH2C(NHCHO)(CO2C2H5)2	1	1	!	862
$\begin{array}{llllllllllllllllllllllllllllllllllll$		$CH_2$ = $CBrCH_2Br$	CH2=CBrCH2C(NHCHO)(CO2C2H5)2	81	NaH	Tolueno	246
$\begin{array}{llllllllllllllllllllllllllllllllllll$		BrCH=CHCH,Br	BrcH=CHCH2C(NHCHO)(CO2C2H5)2	I		1	862
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		BrCH=CHCH,Br	BrCH=CHCH,C(NHCHO)(CO,C,H,),	73	NaH	(CH <sub>3</sub> ) <sub>2</sub> NCHO	860
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Cl2C=CHCH2Br	Cl <sub>2</sub> C=CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	83	NaH	(CH <sub>3</sub> ),NCHO	860
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		HC CCH,Br	HC=CCH,C(NHCHO)(CO,C,H,),	82	NaH	C,H,	246
		B1CH2CH—CH2	BrCH2CHCH2C(NHCHO)CO2C2H3	l	I	, ,	436
n.C <sub>4</sub> H <sub>3</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>1</sub> *         37         NaOCH <sub>3</sub> CH <sub>3</sub> OH           n.C <sub>4</sub> H <sub>3</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> 62         NaOC <sub>2</sub> H <sub>5</sub> Ethanol           CH <sub>3</sub> CCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> *         47         NaOC <sub>2</sub> H <sub>5</sub> Ethanol           CH <sub>3</sub> O <sub>4</sub> CCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> *         47         NaOCH <sub>3</sub> CH <sub>3</sub> OH           CH <sub>2</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub> *         53         NaOC <sub>2</sub> H <sub>5</sub> Ethanol           CH <sub>2</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub> 80         NaH         C <sub>6</sub> H <sub>6</sub> Diethyl (3-thenyl)formamidomalonate         80         NaH         C <sub>6</sub> H <sub>6</sub> Diethyl (3-thenyl)formamidomalonate         93         NaH         CH <sub>3</sub> ) <sub>2</sub> NCHO           C <sub>6</sub> H <sub>5</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> *         75         NaOCH <sub>3</sub> CH <sub>3</sub> OH           p-CH <sub>3</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> *         73         NaOCH <sub>3</sub> CH <sub>3</sub> OH		>º					
n-C <sub>4</sub> H <sub>2</sub> C/HCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), n-C <sub>4</sub> H <sub>3</sub> C/HCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), n-C <sub>4</sub> H <sub>3</sub> C/HCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), cH <sub>2</sub> C(HCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), cH <sub>2</sub> C(HCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), cH <sub>2</sub> C(HCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), cH <sub>3</sub> C(HCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), cH <sub>2</sub> C(HCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), cH <sub>2</sub> C(HCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), cH <sub>2</sub> C(HCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), cH <sub>2</sub> C(HCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(HCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> CH <sub>3</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(H <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )), na <sub>0</sub> C(H <sub>2</sub> CH <sub>2</sub> C(H <sub>2</sub>		n-C,H,Br	* CHO CONCHUNCTION *	6	N. OCH	OTT OTT	000
CH3-C(CH2,C(NHCHO)(CO <sub>2</sub> CH3)2*  CH3-CH(CH2,AC(NHCHO)(CO <sub>2</sub> CH3)2*  CH3-C(CH2,C(NHCHO)(CO <sub>2</sub> CH3)2*  CH3-CH3-C(NHCHO)(CO <sub>2</sub> CH3)2*  CH4-CH3-C(NHCHO)(CO <sub>2</sub> CH3)2*  CH2-CH4-C(NHCHO)(CO <sub>2</sub> CH3)2*  CH4-CH3-C(NHCHO)(CO <sub>2</sub> CH3)2*  CH4-CH3-C(NHCHO)(CO <sub>2</sub> CH3)2*  Diethyl (3-thenyl)formamidomalomate  Diethyl (3-thenyl)formamidomalomate  Diethyl (3-thenyl)formamidomalomate  C <sub>6</sub> H <sub>5</sub> CH <sub>5</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> )2*  T <sub>6</sub> NaOCH <sub>3</sub> C <sub>7</sub> H <sub>9</sub> CH3-NCHO  C <sub>8</sub> H <sub>5</sub> CH <sub>4</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>3</sub> CH <sub>3</sub> )3*  T <sub>7</sub> NaOCH <sub>3</sub> CH3-NCHO  C <sub>8</sub> H <sub>5</sub> CH <sub>4</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>3</sub> CH <sub>3</sub> )3*  T <sub>8</sub> NaOCH <sub>3</sub> CH3-CH3-CH3-CH3-CH3-CH3-CH3-CH3-CH3-CH3-		n-C,H,Br	**C.H.CVHCHCHONCO C.H.)	9	NEOCH3	CHICH	803
CH <sub>3</sub> O <sub>5</sub> CCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> Ch <sub>3</sub> ) <sub>3</sub> *  CH <sub>3</sub> O <sub>5</sub> CCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub> *  CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> Ch <sub>3</sub> ) <sub>3</sub> *  CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> Ch <sub>3</sub> ) <sub>2</sub> *  CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> Ch <sub>3</sub> ) <sub>2</sub> *  Diethyl (3-thenyl)formamidomalonate biethyl (3-thenyl)formamidoma		"a ' HU/HU HU	71	70	NACCITIS	Ethanol	863
CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> CH <sub>2</sub> CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> Diethyl (3-thenyl)formamidomalonate  To Nah  CH <sub>3</sub> )  CH <sub>2</sub> )  CH <sub>3</sub> CH <sub>2</sub> CH <sub>3</sub> OH  CH		Broth Co CH	CH O COII CONTRIBUTED (CO.C.H.5)2	26	$NaOC_2H_5$	Ethanol	864, 437
CHCH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> 53 NaOC <sub>2</sub> H <sub>5</sub> Ethanol CH <sub>2</sub> Diothyl (3-thenyl)formamidomalonate Diothyl (3-thenyl)formamidomalonate Diothyl (3-thenyl)formamidomalonate C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> *  p-CH <sub>3</sub> CH <sub>5</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>3</sub> *  73 NaOCH <sub>3</sub> CH <sub>3</sub> OH  CHOPH		CH2	CH3. CH3.	41	$NaOCH_3$	снзон	863
CH <sub>2</sub> / Diothyl (3-thenyl)formamidomalonate Diothyl (3-thenyl)formamidomalonate Diothyl (3-thenyl)formamidomalonate Diothyl (3-thenyl)formamidomalonate C <sub>6</sub> H <sub>2</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> *  75 NaOCH <sub>3</sub> CH <sub>3</sub> OH  77 NaOCH <sub>3</sub> CH OH		CHCHabr	CHCH2C(NHCHO)(CO2C2H2),	53	NaOC.H.	Ethanol	864
Diethyl (3-thenyl)formamidomalonate Diethyl (3-thenyl)formamidomalonate Diethyl (3-thenyl)formamidomalonate Diethyl (3-thenyl)formamidomalonate C <sub>6</sub> H <sub>3</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> *  75 NaOCH <sub>3</sub> CH <sub>3</sub> OH  77 NaOCH <sub>3</sub> CH OH		CH <sub>2</sub>			3		500
Diethyl (3-thenyl) formamidomalonate 80 NaH Toluene Diethyl (3-thenyl) formamidomalonate 93 NaH $(CH_3)_1NCHO$ $C_6H_5CNHCHO)(CO_2CH_5)_2*$ 75 NaOCH, $CH_3OCH_3CNHCHO)(CO_2CH_3)_**$ 73 NaOCH, $CH_3OCH_3CH_3CH_3CH_3CH_3CH_3CH_3CH_3CH_3CH_3$		3-Bromomethylthiophene		80	NaH	$C_6H_6$	246
Dicthyl (3-thenyl)formamidomalonate 93 $NaH$ (CH <sub>3</sub> ) <sub>2</sub> NCHO $C_6H_5C(NHCHO)(CO_2CH_3)_2*$ 75 $NaOCH_3$ CH <sub>3</sub> OH $p$ -CH <sub>5</sub> O $C_6H_4CH_4$ CH <sub>4</sub> CH <sub>5</sub> C(NHCHO)(CO <sub>5</sub> CH <sub>4</sub> ),* 73 $NaOCH_4$ CH OH		2 Branch of the control of the contr		80	NaH	Toluene	246
$C_{c}H_{c}CH_{c}C(NHCHO)(CO_{c}CH_{c})_{c}^{**}$ 75 NaOCH, $CH_{c}OH_{c}$ $p\cdot CH_{c}OC_{c}H_{c}C(NHCHO)(CO_{c}CH_{c})_{c}^{**}$ 73 NaOCH, $CH_{c}OH_{c}$		C H CH CH		93	NaH	(CH,),NCHO	246
p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCHO)(CO <sub>2</sub> CH <sub>3</sub> ),* 73 NaOCH, CH <sub>2</sub> OH		n.CH OC II OII O	C,H,CH,C(NHCHO)(CO,CH,),*	75	NaOCH3	CH,OH	863
17 CTTO CTTO		Daniel Control	. ,	73	NaOCH,	CH, OH	883

Note: References 577-1080 are on pp. 322-331.
• The dimethyl ester was used in this experiment.

235, 232

2thanol

NaOC,H. NaOC2H 5

> > 20 09 ∧

 $CH_3S(CH_2)_2C(NHCOCH_3)(CO_2C_2H_5)_2$  $CH_3S(CH_2)_2C(NHCOCH_3)(CO_2C_2H_5)_2$ 

i.C3H,C(NHCOCH3)(CO2C2H3)2

n-C3H,C(NHCOCH3)(CO2C2H3)2

3thanol

232,867

64:4

534

998

\*.C,H,OH

NaOC,H9-t NaOC2H5  $NaOC_2H_5$ 

Sthanol Ethanol

 $C_6H_{\frac{1}{8}}$ 

NaOC,H 5

CICH=CHCH,C(NHCOCH,)(CO,C,H,), CH2=CHCH2C(NHCOCH3)(CO2C2H3)2

CICH=CHCH2CI

CH,COCH,Br

CH2-CHCH,Br

i.C,H,Br

CH3S(CH2),CI CH<sub>3</sub>S(CH<sub>2</sub>)<sub>2</sub>CI

n-C<sub>3</sub>H<sub>4</sub>Br

CH,COCH,C(NHCOCH,)(CO,C,H,J),

TABLE II-Continued

ALKYLATION OF CHIORO., NITRO., AMINO. AND ACYLAMINO-MALONIC ESTERS, XCH(CO2R)2 (The diethyl ester was used unless otherwise specified.)

Referonco 246 246862 865  $23_{2}$ 232 246 Polueno Solvent Toluone Toluone Ethanol 3thanol Ethanol Xylenoļ NaOC2H5 NaOC2H5 NaOC<sub>2</sub>H<sub>5</sub> Baso NaH NaH NaH e Z 1 Yield, % % 8 1 # 96 80 Diethyl (3-nitro-4-methoxybenzyl)-CH=CHC(NHCHO)(CO2C2H2)2 (C,H5)2CHC(NHCHO)(CO2C2H5)2 Diethyl (2,4-dimethylbenzyl). C2H3C(NHCOCH3)(CO2C2H6)3 CH3C(NHCOCH3)(CO2C2H3)2 CH3C(NHCOCH3)(CO2C2H5)2 Diethyl (1-naphthylmethyl)-(C2H3O2C)2C(NHCHO)CH2formamidomalonato formamidonnalonato formamidomalonato BrCH == CHCH2C(NHCHO)-3.Nitro-4.mothexybonzyl 2,4.Dimethylbenzyl Alkylating Agent -Chloromothylnaphthaleno (CO2C2H3)2 (C,H,),CHBr chlorido chlorido (CH<sub>3</sub>)<sub>2</sub>SO<sub>4</sub>  $C_2H_5Br$  $C_1 - C_2$  $CH_3I$ CH3CONH HCONH (cont.)

232 860 860 870 870 870 870 870		Ethanol Ethanol Ethanol Toluene Ethanol Toluene Ethanol	NaOC,H's NaOC,H's NaOC,H's NaOC,H's NaOC,H's NaOC,H's	60-70 88 87 71 67 85 60 90	n-C <sub>3</sub> H <sub>11</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Diethyl acetamido(furfuryl)malonate Diethyl acetamido-(2-thenyl)malonate Diethyl acetamido-(2-thenyl)malonate Diethyl acetamido-(3-thenyl)malonate Diethyl acetamido-(3-thenyl)malonate Diethyl acetamido-(5-bromo-2-thenyl) malonato Diethyl acetamido-(5-bromo-3-thenyl) malonate Ethyl acetamido-(2-bromo-3-thenyl) nulonate Ethyl acetamido-x-c-arberthaxy-β- (1-methyl-5-imidaeakyl)propionato	C <sub>5</sub> n-C <sub>5</sub> H <sub>11</sub> Br 2-Chloromethyllturun Diot 2-Chloromethylthiophene 2-Chloromethylthiophene 3-Bromomethylthiophene 5-Bromomethylthiophene 5-Bromon-2-bromomethyl- thiophene 1-Bromo-3-bromomethyl- thiophene 1-C-Bromo-3-bromomethyl- thiophene 1-C-Bromo-1-C-Bromo
446	nol	Ethanol	NaOC <sub>2</sub> H,	50	metnyt)matonate 2-Amino-3-(2-thiazolyl)propionie acid	2.Chloromethylthiazole
447 450, 446		Ethanol Ethanol	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	53 FS	NC(CH <sub>2</sub> ) <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyl acetamido-(4-thiazolyl-	Cl(CH <sub>2</sub> ) <sub>3</sub> CN 4-Chloromethylthiazole
232	nol		$NaOC_2H_5$	ļ	$\mathrm{CH}_2 = \mathrm{C}(\mathrm{CH}_2)\mathrm{CH}_2\mathrm{C}(\mathrm{NHCOCH}_3)(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	CH;=C(CII,)CH,CI
868 442	ene nol	Toluene Ethanol	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	88 80	$(\mathrm{CH}_4)_2\mathrm{N}(\mathrm{CH}_2)_2\mathrm{C}(\mathrm{NHCOCH}_3)(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_3)_2$ $\mathrm{CH}_3\mathrm{CH}=\mathrm{CHCH}_2\mathrm{C}(\mathrm{NHCOCH}_3)(\mathrm{CO}_3\mathrm{C}_2\mathrm{H}_3)_2$	$(CH_3)_2N(CH_2)_2CI$ $CH_3CH == CHCH_2CI$
235, 232			NaOC2H3	97	$i.C_1H_0C(NHCOCH_3)(CO_2C_2H_3)_2$	i.C.III,Br
235 232	nol	Ethanol	NaOC,H,	1	n·C,H,C(NHCOCH,)(CO,G,H,),	n·C,H,I
442, 232,		Ethanol	$NaOC_2H_5$		".C,H,C(NHCOCH,)(CO,C,H,);	n-C,III,Br-NaI

### TABLE II-Continued

Alkylation of Chloro-, Nitro-, Amno- and Acylamino-malonic Esters,  $\mathrm{XCH}(\mathrm{CO_2R})_2$ diethyl ester was used unless otherwise specified.)

Refer-	onco	133 144 148 148 148 148 148 148 148 148 148	133	#12	49, 456
	Solvent	Ethanol Ethanol Ethanol Ethanol Ethanol Ethanol Ethanol Ethanol Ethanol Ethanol	Ethanol Ethanol Ethanol	Ethanol	C,III,
	Baso	NnOC;II; NnOC;II; NnOC;II; NnOC;II; NnOC;II; NnOC;II; NnOC;II; NnOC;II; NnOC;II; NnOC;II; NnOC;II;	NaOC,II; NaOC,II; NaOC,II;	NaOC,II,	NaOC, II,
Vield.	%	82 89 68 68 76 81 81 88 89 89 89 89 89 89 89 90 90 90	182	82	11
(The diethyl ester was used unless office and Vield	Product	n.C,H <sub>13</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), C <sub>6</sub> H <sub>3</sub> CH <sub>4</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), o-FC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), m-FC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), p-FC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), p-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), g <sub>2</sub> +Cl <sub>3</sub> C <sub>3</sub> H <sub>2</sub> CH <sub>3</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), g <sub>2</sub> +Cl <sub>3</sub> C <sub>4</sub> H <sub>2</sub> CH <sub>3</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), p <sub>2</sub> -C,NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), p <sub>2</sub> -C,NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), p <sub>2</sub> -C,NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), p <sub>2</sub> -C,NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), p <sub>2</sub> -H <sub>3</sub> NC <sub>6</sub> H <sub>4</sub> CH <sub>3</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ), p <sub>2</sub> -H <sub>3</sub> NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(NHCOCH <sub>4</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ),	$n.C_{4H_1}$ ,C(NIICOCH <sub>1</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> ), $C_{4H_3}$ S(CH <sub>4</sub> ),CH(NH <sub>4</sub> )CO <sub>4</sub> H 2.Amino-3-(3-nitro-4-methylphenyl)-	propionie neid Diethyl acetamido-(2-fluoro-4-	methoxylenzyl)malonato C <sub>4</sub> H <sub>5</sub> COCH <sub>2</sub> C(XHCOCH <sub>3</sub> )(CO <sub>4</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>3</sub>
(Th	Alkylating Agent	07, n-C,H <sub>13</sub> Br C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cl o-FC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl m-FC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl c <sub>7</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl c <sub>7</sub> Cl c <sub>7</sub> H <sub>4</sub> CH <sub>2</sub> Cl c <sub>7</sub> Cl c <sub>7</sub> H <sub>4</sub> CH <sub>2</sub> Cl c <sub>7</sub> Cl c <sub>7</sub> H <sub>7</sub> CH <sub>2</sub> Cl c <sub>7</sub> Cl c <sub>7</sub> H <sub>7</sub> CH <sub>2</sub> Cl c <sub>7</sub> Cl c <sub>7</sub> H <sub>7</sub> CH <sub>2</sub> Cl c <sub>7</sub> Cl c <sub>7</sub> H <sub>7</sub> CH <sub>2</sub> Cl c <sub>7</sub> C	$O_s$ $n$ · $C_sH_1r^I$ $C_sH_s(S(CH_2)_sG)$ $3$ ·Nitro- $4$ -methylbenzyl	ehloride 2.Fluoro-4-methoxybenzyl	chleride C,H,COCH,Br
	×	(Cont.)			

o-O <sub>2</sub> NG <sub>6</sub> H <sub>4</sub> COCH <sub>2</sub> Br o-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COCH <sub>2</sub> Br 5-Chloromethyl-1-	o.O <sub>2</sub> NC <sub>6</sub> H <sub>3</sub> COCH <sub>2</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> o.O <sub>2</sub> NC <sub>6</sub> H <sub>3</sub> COCH <sub>3</sub> C(NHCOCH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> 2-Amino-3-(1-isopropyl-5-imidazolyl)-	41 19 44	NaOC2Hs NaOC2Hs NaOC2Hs	Ethanol (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO Ethanol	456 49 443
isopropylimidazole hydrochlorido	propionic acid				1
1-Chloromethyl- benzimidazole	2-Amino-3-(1-benzimidazolyl)propionic acid	1	NaOC <sub>2</sub> H <sub>s</sub>	Ethanol	455
hydrochlorido					1
2-Chloromethyl-	Diethyl acetamido-(2-benzimidazolyl-	65	$NaOC_2H_5$	Ethanol	455
benzimidazole hydrochloride	mcthy!)malonate				
ر ر					
$n$ -C, $\mathbf{H_{19}Br}$	$n \cdot C_{\bullet}H_{1,0}C(NHCOCH_{\bullet})(CO,C,H_{\epsilon}),$	1	NaOC,H,	Ethanol	232
2-Ethoxy-5-nitrobenzyl	Diethyl acetamido-(2-othoxy-5-	82	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	448
chloride	nitrobenzyl)malonate				
2.Bromo.3.bromo.	Diethyl acctamido-(2-bromo-3-	73	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	440
methylcoumarone	coumaronylmethyl)malonate				
2-Chloremethyl-4-	Ethyl 2-acetamido-3-(4-methyl-2-	40	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	455
methylbenzimidazole hydrochloride	benzimidazolyl)propionate				
2-Chloromethyl-5-methyl-	Within 9 postomide 9 (5 method 9	,	TT 00 - 74	Ta. L	1
benzimidazole	benzimidazolyl)propionata	00	NEOC2TS	Eduanoi	400
hydrochloride					
$G_{10}$					
eta-3-Indolylethyl bromide	Diethyl acetamido-[\(\beta(3\)-indolyl)-	58	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	441
on in the second	etnyl]malonate				
o-Culorometnyl-1. eyelohexylimidazole hydrochleride	2.Amino-3.(1-cyclohexyl.5.imidazolyl). propionic acid	49	$NaOC_2H_{\delta}$	Ethanol	443

Note: References 577-1080 are on pp. 322-331.

## TABLE II-Continued

Alkylation of Chloro-, Nitro-, Amino- and Acylamino-malonic Esters,  $\mathrm{XCH}(\mathrm{CO_2R})_2$ (The diethyl ester was used unless otherwise specified.)

Rofer- onco 443	465	439	440	£ <del>1</del> 4	454	438
Solvont Ethanol	Ethanol	I	Ethanol	Ethanol	Ethanol-	Ethanol- dioxano
Baso NaOC.H.	ca. 40 NnOC,Hs	i	NaOC2Hs	NaOC <sub>2</sub> H <sub>s</sub>	NaOC,H,	$NnOC_2H_s$
Yiold, %	ca. 40	i	93	45	74	84
	2.Amino-3-(1-plionyl-b-imidazolyl)- propionie acid Ethyl 2-acetamido-3-(5,6-dimothyl-2- benzimidazolyl)propionato	C,H,CH(CO,C,H,)CH,C(NHCOCH,)	А	mothyl)nnlonnto 2.Amino-3-(1-benzyl-5-imidazolyl)• propionic acid	Diethyl acctamido-[4-(4-nitro-	phenylsullonyl)bonzyl Jmalonato Diethyl acetamido-[3,5-dijodo-4- (4-methoxyphenylsulfonyl)bonzyl]- malonato
Allsylating Agent	5.Chloromethyl-1. phenylimidazolo hydroehlorido 2.Chloromethyl-5,6. dimethylbenzimidazolo hydroehlorido	$G_{11}$ $G_0H_2\mathbb{C}H(\mathbb{CO}_2\mathbb{C}_2H_6)\mathbb{C}H_2\mathbb{B}r$	1-ChlorometlyInaphthaleno	5.Chloromethyl·1· benzylimidazolo hydrochlorido	$C_{13}$ – $C_{14}$ 4-(4-Nitrophenyl-	sulfonyl)bonzyl bromido 3,5-Diiodo-4- (4-methoxyphenyl- sulfonyl)benzyl chlorido
×	CH <sub>3</sub> CONH (Cont.)					

233 233 459 458 233 453	871 467 460 466, 465 462, 435 462, 236, 463 461 462 869	462 236, 462
Ethanol Ethanol Ethanol Ethanol Ethanol Ethanol	C.H. CICH,CO,C,H, Xylene None None None None None	None None
NaOC,Hs NaOC,Hs NaOC,Hs NaOC,Hs NaOC,Hs NaOC,Hs	Na NaOC,H, NaOC,H, NaOC,H, NaOC,H, NaOC,H, NaOC,H,	NaOC <sub>2</sub> H <sub>5</sub> Na
66 74 88 90 17 7	73 95-99 81 81 76-80 90 50 50 75-80 93	75–80 75
C <sub>6</sub> H <sub>5</sub> CONHC(C <sub>3</sub> H <sub>7</sub> -i)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ), C <sub>6</sub> H <sub>5</sub> CONHC(C <sub>1</sub> H <sub>6</sub> -i)(CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ), C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(NHCOC <sub>6</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ), C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ),C(NHCOC <sub>6</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ), 2-Amino-3-(2-pyridyl)propionic acid C <sub>6</sub> H <sub>5</sub> CONHC(CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ), p-HOC <sub>6</sub> H <sub>4</sub> (CH <sub>2</sub> ),CCH(NH <sub>2</sub> )CO <sub>2</sub> H	CH <sub>3</sub> OCH <sub>2</sub> C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>7</sub> H <sub>5</sub> ); C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>7</sub> H <sub>5</sub> ); (C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C)C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)CH <sub>2</sub> S. CH <sub>2</sub> C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ); CH <sub>3</sub> C(CH <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ); CH <sub>2</sub> =CHCH <sub>2</sub> C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ); CH <sub>2</sub> =CHCH <sub>2</sub> C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ); C(C <sub>6</sub> H <sub>5</sub> O <sub>2</sub> C)C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ); C(C <sub>6</sub> H <sub>5</sub> O <sub>2</sub> C)C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ); C(C <sub>6</sub> H <sub>5</sub> O <sub>2</sub> C)C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ); NC(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ); Diethyl phthalimido(2-thenyl)malonate	malonate C <sub>6</sub> H <sub>2</sub> CH <sub>2</sub> C(C <sub>6</sub> H <sub>4</sub> O <sub>2</sub> N)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyl (γ-phthalimidopropyl). phthalimidomalonate
C <sub>2</sub> -C <sub>8</sub> i.C <sub>1</sub> H <sub>1</sub> I i.C <sub>1</sub> H <sub>2</sub> I clCH <sub>2</sub> C <sub>2</sub> C <sub>2</sub> H <sub>5</sub> Br(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> 2-Chloromethylpyridino C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C <sub>2</sub> C <sub>4</sub> H <sub>5</sub> p-HOC <sub>6</sub> H <sub>4</sub> (CH <sub>2</sub> ) <sub>2</sub> Br	Phthal- imido (=C <sub>8</sub> H <sub>1</sub> O <sub>2</sub> N) CH <sub>3</sub> OCH <sub>2</sub> Cl ClOH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ClCH <sub>2</sub> SCH <sub>2</sub> Cl CH <sub>4</sub> S(CH <sub>2</sub> ) <sub>2</sub> Cl CH <sub>2</sub> ECHCH <sub>1</sub> I Br(CH <sub>2</sub> ) <sub>3</sub> Cl CH <sub>2</sub> ECHCH <sub>2</sub> I Br(CH <sub>2</sub> ) <sub>3</sub> Br Q <sub>4</sub> -C <sub>11</sub> C <sub>2</sub> H <sub>3</sub> S(CH <sub>2</sub> ) <sub>2</sub> Cl Cl(CH <sub>2</sub> ) <sub>3</sub> Cl	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cl γ-Bromopropylphthalimide
C,H,CONH	Phthal- imido (=C <sub>s</sub> H <sub>1</sub> O <sub>2</sub> )	, , , , , , , , , , , , , , , , , , ,

Note: References 577-1080 are on pp. 322-331.

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82 571 872 331

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571 205

#### TABLE III

874, 172 Refer-Cthanol Ethanol Ether Toluene Ethanol Ethanol Ether None Ethanol Ethanol Ether Solvent  $C_{\mathbf{g}}\Pi_{\mathbf{g}}$ Ether Ether Ether NaOC<sub>2</sub>H<sub>5</sub> NaOC<sub>2</sub>H<sub>5</sub> NaOC<sub>2</sub>IIs NaOC<sub>2</sub>II<sub>5</sub>  $NaOC_2 H_5$   $NaOC_2 H_5$ Alkylation of Monoalkylmalonic Esters,  $\mathrm{R'CH}(\mathrm{CO}_2\mathrm{R})_2$ Base (The diethyl ester was used unless otherwise indicated.) KOII e Z Z. ď ž ž Yleld, 13 12 22 22 얾 Br\_c'H C(CH\_3)(CO\_2C\_2H\_3)2 and (C\_2H\_3)(CO\_2C\_2H\_3)2 (C\_2H\_3)(CH\_  $(c_{2\Pi_{5}}o_{2}\breve{c})_{2}C(c\tilde{\Pi}_{3})c\tilde{\Pi}\breve{c}lC(C\Pi_{3})(CO_{2}C_{2}\Pi_{5})_{2}$ Cl2CHCHCH3)(CO2C2H3)2 and (C2H3O2C)2CH3)2  $\begin{array}{l} n\text{-}C_3\Pi_1\text{C}(\text{C}\Pi_3)(\text{CO}_2\text{C}_2\Pi_3)_2 \\ n\text{-}C_3\Pi_1\text{C}(\text{C}\Pi_3)(\text{CO}_2\text{C}_2\Pi_3)_2 \\ \text{C}_2\Pi_5\text{SCH}_2\text{C}(\text{C}\Pi_3)(\text{CO}_2\text{C}_2\Pi_5)_2 \end{array}$  $B_{T}(CII_{2})_{2}C(CII_{3})(CO_{2}C_{2}II_{3})_{2}$ Clacific (Clis)(CO2C211s)2 and  $\begin{array}{c} C_2\Pi_5(C\Pi_3)(CO_2^{C_2\Pi_5})_2 \\ C\Pi_5SC\Pi_2(C\Pi_3)(CO_2^{C_2\Pi_5})_2 \\ CI(C\Pi_2)_2C(C\Pi_3)(CO_2^{C_2\Pi_5})_2 \end{array}$  $\mathrm{Br}(\mathrm{CH}_2)_2\mathrm{C}(\mathrm{CH}_3)(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$  $\operatorname{CH}_2[\operatorname{C}(\operatorname{CH}_3)(\operatorname{CO}_2\operatorname{C}_2\operatorname{H}_5)_2]$ (CH2C(CH3)(CO2C2H5)2 CII2C(CII3)(CO2C2II3)  $(CII_3)_2C(CO_2C_2II_5)_2$  $(CII_3)_2C(CO_2C_2II_6)_2$ Product Alkylating CH2BrCH2Br CH<sub>2</sub>BrCH<sub>2</sub>Br  $C_2H_5SCH_2CH$ C2H5I CH3SCH2CI CH2CICH2Br Agent Not stated n- $C_3\Pi_7I$ CHIBr3 CH212 CIICI3 CIICI3 CIII3 CII

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CH,  $\vec{c}$ 

125 571	556 556	870, 241 653, 161	653	571	205	533	ï	100	<u>.</u>	100	3 1	2.2		223, 702		752	334	ç	878		551	247	551	553	223, 162		872, 162, 223
1.00	629	653	9	ru i	61 1	ഥ			a i	0 -	<b>-</b> , (	<b>20</b>		253			က	•	90		ū	C1	r.	r.	223		872, 2
Tolucne Ethanol	Ether	Ether	$C_6\Pi_{fi}$	1	Ether	Ethanol	1000	ECHANOL	Ethanol	Ethanol Tolucia	Tomene	None		Ethanol		сизон	Ethanol		Į		Ethanol	$c_{\rm eH_6}$	Ethanol	Toluene	Ethanol		Nonc
$ m NaOC_2H_5$ $ m NaOC_2H_5$	Na -	Na	Na	Na	Na	$NaOC_2H_5$		NaOC2H5	NaOC2H5	NaOC, H5	NaUC <sub>2</sub> II <sub>5</sub>	Na		$NnOC_2II_5$		NaOCHa	NaOC <sub>2</sub> H <sub>5</sub>	•	l		$NaOC_2H_5$	Na	$NaOC_2H_5$	NaOC, H5	NaOC <sub>2</sub> H <sub>5</sub>		Na
1.1	<del>2</del>	87-89	1	1	43	١		١	١	١	١	١		37		1-1	18		Cood		!	83	1	70-90	56		57
$C_2H_5SCH_2C(CH_3)(CO_2C_2H_5)_2$ $i:C_1H_1C(CH_3)(CO_5C_5H_5)_2$	nr(CH <sub>2</sub> ),C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (CH <sub>3</sub> ),C(NO <sub>2</sub> )C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	$CH_2 = CHCH_2C(CH_3)(CO_2C_2H_5)_2$	Diethyl a-carbethoxy-a-methylsuccinate	n-C,H,C(CH),(CO,C,H5),	C, H, SCH(CH,)C(CH,3)(CO,CH,3).*	CIT3CCI=CHCIT2C(CH3)(CO2C2H5)2		n-C <sub>5</sub> H <sub>11</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>6</sub> ) <sub>2</sub>	$n \cdot C_3 H_7 \text{CII}(\text{CH}_3) \text{C}(\text{CH}_3) \text{C}(\text{CO}_2 \text{C}_2 \text{H}_5)_2$	i.C <sub>5</sub> II <sub>11</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub>	n-C <sub>4</sub> II <sub>9</sub> SCH <sub>2</sub> C(CII <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub>	Dictiyl a,a'-dimethyl-a-	earbethoxysuccinate	Diethyl a, a'-dimethyl-a-	earbethoxysuccinate	$(CH_3O_2C)_2CHCH(CO_2CH_3)_2^*$ and $(CH_3O_2C)_2CH_3O_2^*$ .	Diethyl (cyclobutylmethyl)-	methylmalonate	Diethyl (a-thenyl)methylmalonate		11-C <sub>6</sub> H <sub>13</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	i-C,H <sub>13</sub> C(CH <sub>3</sub> )(CO,C,H <sub>5</sub> ) <sub>2</sub>	n-C,H,CH(CH,3)C(CH,3)(CO,C,H,5)2	$n$ -C,H $_9$ S(CH $_2$ ) $_2$ C(CH $_3$ )(CO $_2$ C $_2$ H $_5$ ) $_2$	Diethyl a-methyl-a'-ethyl-a-	carbethoxysuceinate	Dicthyl a,a,a'-trimethyl-a'- carbethoxysuccinate
C2H5SCH2Cl	Dr(CH <sub>2</sub> ) <sub>3</sub> Br (CH <sub>2</sub> ) <sub>2</sub> ClNO <sub>2</sub>	$CII_2 = CHCH_2CI$	$CICH_2CO_2C_2H_5$ $CICH_2CO_2C_2H_5$	Ca Not stated	C.II.SCII(GIL.)CI	CH <sub>3</sub> CCI = CHCH <sub>2</sub> Cl	ప	n-C,II,1Br	$n \cdot C_3 \Pi_1 \hat{C} \Pi (C\Pi_3) \Pi_r$	i-CoIIIBr	n-CAII SCII CI	CII, CII BrCO, C, H,	•	$\mathrm{CH_3CHDrCO_2C_2H_5}$		CICII(CO2CH3)2	Cyclobutylmethyl tosylate		a-Chloromethylthiophene	$G_{6}$	$n \cdot \mathbf{C_6H_{13}Br}$	÷-C <sub>6</sub> 11 <sub>13</sub> 1	$n\text{-}\mathrm{C}_4\mathrm{H}_9\mathrm{CH}(\mathrm{CH}_3)\mathrm{Br}$	"·C,II,S(CH2)2C1	$c_2 H_s \mathrm{CHBrCO_2} c_2 H_5$	TO OD-US (CHS)	C113/2CE1C03C2H5

Note: References 577-1080 are on pp. 322-331, The dimethyl ester was used in this experiment,

# TABLE III-Continued

Alkylation of Monoalkylmalonic Esters,  $\mathrm{RCH}(\mathrm{CO}_2\mathrm{R})_2$ (The diethyl ester was used unless otherwise indicated.)

It' ('ll') (('ont.)

Refer-	ence 319 319, 150	855	758 758	334	3:34	334	33-1	015	879	551	880	126	426	881 873, 758
	Solvent Ethanol	Ethanol	Ethanol Ethanol	Ethanol	Ethanol	Ethanol	$n$ - $C_4\Pi_9$ O $\Pi$	Ethanol	Elhanol	Ethanol	Ethanol	Toluene	$C_6II_6$	Xylene Toluene
	Basc NaOC <sub>2</sub> U <sub>5</sub> NaOC <sub>2</sub> U <sub>5</sub>	NaOC <sub>2</sub> II <sub>s</sub>	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	NaOC <sub>2</sub> II <sub>5</sub>	NaOC2118	NaOC <sub>2</sub> II <sub>5</sub>	Na0C,119-2	NaOC <sub>2</sub> H <sub>5</sub>	NaOC,IIs	NaOC, II.	NaOC <sub>2</sub> II	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	×	K Na
	Yleld. % 73 >60	æ	Poor	1 99	26	1	65	1	83	:	9	5 70–90	53	65
(The diethyl ester was used unless otherwise mercen-	Product Dictiy1 (2-cyclohexeny))methylmalonate Dictiy1 (2-cyclohexeny))methylmalonate	- 's-later lacerous - x'-mellyl-x'-	nemy actoriography enriched enriched by the confection of the conf	$\begin{cases} (C_2 \Pi_1 G_2 C)_2 C = C(CO_2 C_2 \Pi_3)_2 \\ (C_2 \Pi_1 G_2 C)_3 C = C(CO_2 C_2 \Pi_3)_2 \end{cases}$	Dietnyt metnyr (* * * * * * * * * * * * * * * * * * *	thenst methyly (2 cy c. ) ethylynalonate ratefully methyllexelohexylmethyl).	malonate District methyl(evolutexyl-	unethyl)nualonate c <sub>6</sub> H <sub>2</sub> CH <sub>2</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	(11 0 00)	n-C <sub>8</sub> II <sub>17</sub> C(CII <sub>3</sub> )(CU <sub>2</sub> C <sub>2</sub> II <sub>5</sub> / <sub>2</sub>	n-C4H, CH(C2H,) CH2-(CH3)(CO2C2: 15,2	(C <sub>2</sub> II <sub>3</sub> O <sub>2</sub> C) <sub>2</sub> C(CII <sub>3</sub> )C(CII <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub> ) <sub>2</sub>	ethylmethylmalonato	cthylimalonate C <sub>6</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> O(CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>
oib off)	MRylating Agent Agent 2-Cyclohevenyl brounide	C <sub>1</sub>	(:C3H;CHHrCO4C3H3 (:CCH(CO4C3H5)3	11rC11(CO <sub>2</sub> C <sub>2</sub> 11 <sub>5</sub> ) <sub>2</sub>	p.(g.Cyclopentenyl)ethyl bromlde	p.(2.Cyclopentenyl)elnyl tosylate	Cyclohexylmelliyi lodide	Cyclohexylmetnyl fodiac C <sub>6</sub> 11 <sub>5</sub> CH <sub>2</sub> Cl	ప్	n-C,111,21	n.C,II,CII(C,II,S)CII,BE	(CH <sub>3</sub> )2CB4CH <sub>2</sub> H <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> CH <sub>3</sub> CH <sub>3</sub> CCH(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> )2	a.Chloroethyleycionexyl sulfido	p-(1-cyctolexeny.)cm3 · bromlde C <sub>6</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>3</sub> Br C <sub>6</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>3</sub> Br

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n-CgIIIgI	$n$ - $C_0H_{10}C(CH_3)(CO_2C_2H_6)_3$	25	100%	Ethanol	885
$Br(CH_2)_3CH(C_2H_5)CO_2C_2H_5$	C2H5O2CCH(C2H5)(CH2)3C(CH3)(CO2C2H5)2 C H OCCH ) CCH MOO.C.H.).	1 1	NaOCH,	CILOII	581
Can CH (CH.) Br	Cells Company Contact Strains	20	Na	$c_{ m e II}_{ m e}$	883
2-CH-C-H-(CH2)-Br	n-CH,C,H,(CH,),C(CH,)(CO,C,H,)	87	Na	$C_6II_6$	416
$p\text{-}\text{CII}_3\text{C}_6\text{II}_4(\text{CII}_2)_2\text{Br}$	p-CII,3C6II,(CII2),2C(CII3)(CO2C2II5)2	35	$NaOC_2H_5$	Ethanol	£23
$G_{10}$				,	i
Geranyl chloride	Diethyl methyl(geranyl)malonate	20	NaOC <sub>2</sub> II <sub>5</sub>	Ethanol	31
C.H.CH.SCH,CH(CH,)Br	$C_n\Pi_sCH_2SCH_2CH(CH_3)C(C\Pi_3)(CO_2C_2H_5)_2$	20	$NaOC_2H_5$	Ethanol	794
β-(2,3-Dimethylphenyl)ethyl	Diethyl methyl-[8-(2,3-dimethylphenyl)-	20	Na	$C_6II_6$	417
promide	ethytjmaionate	Š		=	
h-(2,4-Dimethylphenyl)ethyl	Diethyl methyl-[\beta-(2,4-dimethylphenyl)-	5	N. P.	91190	114
bromide	ethyl)malonate		;	•	
$p \cdot c_2 \Pi_s C_6 \Pi_s CO C \Pi_2 C I$	$p$ - $c_2 H_s C_6 H_4 CO C H_2 C (C H_3) (CO_2 C_2 H_5)_2$	12	Na	Ether	07.7
Calisch BrcO2C2H5	C6H5CH(CO2C2H3)C(CH3)(CO2C2H5)2	45	Na	None	583
m-Carbethoxybenzyl chloride	Diethyl methyl-(m-earbethoxybenzyl).	1	1	i	230
	malonate				
$ heta ext{-Bromoethylphthallmlde}$	Diethyl methyl-( $\theta$ -phthallmidoethyl)-malonate	40-46	Na	$C_6H_6$	884
$c_{11}$					
Chloromethyltetralln+	Diethyl methyldetrahydronanhthyl.	5.1	, N	H	410
	methylmalonate	;		9,,9	277
$\alpha$ -Chloromethylnaphthalene	Dietliyl methyl-(a-naphthylmethyl)-	11	$NaOC_2H_5$	Ethanol	882, 886
eta-Chloromethylnaplıtlıalene	Diethyl methyl-(8-naphthylmethyl)- malonate	1	1	1	880
$C_{13}$ - $C_{24}$					
$n\text{-}\mathrm{C}_{12}\mathrm{H}_{25}\mathrm{X}$	n-C <sub>12</sub> H <sub>25</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ),	ł	1	1	887
n-C <sub>13</sub> H <sub>27</sub> X‡	n-C <sub>13</sub> H <sub>27</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	1	$NnOC_2H_5$	Ethanol	888
$n ext{-} ext{C}_{14} ext{H}_{29} ext{X}_{f  au}^{\star}$	n-C14H29C(CH3)(CO2C2H5)2	1	1	1	887

Note: References 577-1080 are on pp. 322-331.
† This halide was probably a mixture of isomers.
‡ The halogen was not specified.



	СИ <sub>2</sub> ВгСИ <sub>1</sub> Вг	$CII_2CII_2C(C_2H_5)CO_2C_2H_5$	1	Na	$C_6H_6$	555
	CH <sub>2</sub> BrCH <sub>4</sub> Br	0	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	172
	BrCII=ClIBr	$\begin{array}{l} \operatorname{BrCH} = \operatorname{CHC}(C_2 \operatorname{H}_5)(\operatorname{CO}_2 C_2 \operatorname{H}_5)_2 \\ \operatorname{3.6.6-Tricarbethoxy-3-oetene} \end{array}$	25 31	Na	Ether	4.
	ີ່	V 11 0 00% 11 0% V 110/0 110	l	ì	١	374
	C1130(C112)2C1	CH3O(CH2)2C(C2H5)(CO2C2H5)2 C.H.OCH-C(C-If+)(CO-C-If+).	1.	Na .	Ether	542
	7 11 SC11 CI	C. II. SCII. C(C. II.)(CO.C. II.)	19	Na	Ether	205
	C.11.SCHC.	C.11.SCII.C(C.11.)(CO.C.11.)	l	$N_2OC_2H_5$	Toluene	125
	CHECOCIFC	CILCOCILC(C,IL)(CO,C,H,),	1	Na	Ether	891
	בון בסבורים	CH,COCH,C(C,115)(CO,C,H5),	1	Na	$c_{ m eH_{ m g}}$	891
	(-C-11-1	i.c.11,C(C,11,)(CO,C,H,),	46 (75) §	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	145
	CH. = CHCH.C	CII,=CIICII,C(C,II,)(CO,C,II,),	20-80	NaOC2H5	Ethanol	558
	CICILAND	C(CII,),C(C,II,)(CO,C,II,),	I	NaOC <sub>2</sub> H <sub>5</sub>	Efhanol	814
	CiCila	I(CII,), C(C, II,)(CO, C, II,),	46	NaOC2H5	Ethanol	36
	Br(CII,),13r	Br(CH,),C(C,H,)(CO,C,H,),	32	Na	$C_6H_6$	537, 656
	Br(C112), Br	Br(CH2)3C(C2H5)(CO2C2H5)2	ı	NnOC2II5	Ethanol	814
	CHA-CCINO.	(CII3)2CNO2C(C2II5)(CO2C2H5)2	40 (65) §	Na	Ether	177
	20110020000	$(CII_3)_2CIIC(C_2II_5)(CO_2C_2H_5)_2$	8 (13)§			
	cin-cicii = chclí <sub>2</sub> ci	$cis\text{-}CiCiI = CIICII_2C(C_2II_5)(CO_2C_2II_5)_2$	70-80	$NaOC_2H_5$	Ethanol	558
	trans-CiCII = CIICII <sub>2</sub> CI	trans-CiCil = CHCil2C(C2H5)(CO2C2H5)2	70-80	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	558, 621
	CH <sub>2</sub> =CCICH <sub>2</sub> Cl	$CH_2 = CCICH_2C(C_2H_5)(CO_2C_2H_5)_2$	10-80	NaOC2H5	Ethanol	899
	7.7					-
	n.C4HgBr	n-C <sub>4</sub> II <sub>8</sub> C(C <sub>2</sub> II <sub>5</sub> )(CO <sub>2</sub> C <sub>3</sub> II <sub>5</sub> ),	ເສ. 80	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	536
	11-0,1191	n-C,11,C(C,11,)(CO,C,11,),	62	NaOC2H5	Ethanol	399, 892
	$(C_1\Pi_0O\cdot n)_2CO$	n-C,11'sC(C211's)(CO2C,11'9-n)2'	42 (68)§	NaOC, Hg-n	$(n \cdot C_4 \Pi_9 O)_2 CO$	890, 330
	CH <sub>3</sub> O(CH <sub>2</sub> ) <sub>3</sub> Ci (C, H <sub>2</sub> O-i),CO	CH <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> * EC.H.C(C-H.MCO-C.H3) b	45 (70)8		Methanol	814
Note: Deferences	Note: Before and no one Obolt 253 seement of the State		6 (24) 21		0.27.67.17.17	000,000
Albier Avergation es	or r=1000 are on phy ozz=101.					

§ Here and In subsequent cases the first figure represents the conversion; the figure in parentheses represents the yield. || The disobutyl ester was used in this experiment.
7 The disobutyl ester was used in this experiment.

· The dimethyl ester was used in this experiment. ; The halogen was not specified.

# TABLE III Continued

Alkymation of Manoalkytanhonic Bettins,  $W(H(CO_2R)_2)$  (The diethyl edge was used unless otherwise indicated.)

Befer	ellee	630, 163	<u>.</u>	855	=	į	212	37.1	503	211	125	126	202	125	195, 803	30.5	0000	ī		653, 161,	891	053, 891	804	400		513,895	101	4-1, 51,	100
į	Solvent	I'thanol	Toluene	Lithanol	Ethanol		Ether	1	Cellerether	Ethanol	Toluche	Toluene	Viller	Polimen	T CHARGA	anamol.	Ethanol	Ether		Ether		C,11,	Ether	C <sub>6</sub> 11,		Ethanol	Toluene	(C.11.0), CO	7. 7. 8.
He'tt.)	Basic	V=00.1L	·	NaOC, II,	NaOC2115		N.	1		X.00.11.	Value 11.	NaOC 1115	Anto-1113	Na	NaOC, IIs	NuOC2115	NaOC, II's	NaNII;		,	1947	Ž	Na	Nn		NaOC <sub>2</sub> 115	Na	NaOC, II,	A.C. 1115
se indher Yield.	è		ê.	9.00	99		2	2	1 8	95 2	5	1	20-50	ï	ı	1	70-80	99			i	1	1 1	ł		20	12	ca, 80	9
(The dicthyl ester was used unless otherwise addiction)		Profilect	C.11.CH(CH(2)YYC3113)YCO1(C1113)1	(611,),(00,011,)(00,011,0)	CH <sub>2</sub> (3(CH <sub>3</sub> )CH <sub>2</sub> (3(C <sub>2</sub> H <sub>3</sub> )CO <sub>2</sub> (3 <sup>1</sup> H <sub>3</sub> )2 CHC - CHCHCH <sub>3</sub> (3(C <sub>2</sub> H <sub>3</sub> )CO <sub>2</sub> (3 <sup>1</sup> H <sub>3</sub> )2		0.)0	".C.11.0C11.C(C,11.)(CO.C.11.)	C.11,0(C11,0);C(C,11,0)(C0,C+11,0)	(5115)6(0)(6115)).((1113)(1015)(113)	c(11, 2010)(c11, 2), c(11, 2) (c11, 2), c11, 2),	1, C. 11, SC11, ('CC-11, )(CO, C, 11, 1),	1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1	(113)(C)(13)(C)(13)(C)(13)	Cally Collection (Cally)	(-(-11-2-01-2-1-3))		(112 (C) -1 (11 C) (C) 12 (C)		0.)	C311303CC112C(C3113)(CO2(C3113)2		C_11_O_C(C_11_C(C_11_0)(CO_C_11_0)_2	C111503CC114CC7115XC042C115X	すること、10~~~10~10~10~10~10~10~10~10~10~10~10~10	VIII OOM II OOM II	2-C_11_1/C(C_111_6/CC_1/211_6/2 7-C_11_C(C_111_/CC)_(*_11_6)*	£C.11,C(C.11,)(CO.C.11,)2	i.c.111,c(c.11,5)CO2(c.11,5);
4L)		100100	* C.	C111,C11C 11,11C	(1115) (115) (115)	til) -ilollo filo	عر	17 11000 00 00		1,2(1,1)(0,1)	1 1 2 11 11 11 11 21 21 21	1,5,5,10,010, 5,110	3.0.11,20.11,00.11	C, 11, >C11(C11, 1)C1	C,11,3C11(C11,3)C1	15,11,501,01	EH, EHCH, SCH, C	ยนุ้งต~-ตเตนุ	(' <sub>2</sub> 11 <sub>5</sub> OCH11sCH <sub>2</sub> 13r		CICIL-CO.C.II.	*	CICHICOICIUS	HrCH,CO,C,H,	131CH 4CO 4C4H3	ย์	n.C.111111	11 11 0 7	1.C, 11, 11

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			ç	. # 202	OJ OJ D J	066 008
	(f-C <sub>5</sub> 1I <sub>11</sub> O) <sub>2</sub> CO	i-C <sub>5</sub> H <sub>11</sub> C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>5</sub> H <sub>11</sub> -t) <sub>2</sub> · ·	3	NaOC.H.	Ethanol	617
	7-03-15-014(CH3)D1	/+)-a-f-H-GH(CH-)C(CaH-)(CO,CaH-)	١	NaOC,H.	Ethanol	549
	(-)	(-).n.C.H.CH(CH.)C(C,H.)(CO,C,H.).	١	NaOC, II,	Ethanol	549
	C.II.).CIIIkr	(G.H.), CHC(C,H.)(CO,C,H.),	1	NaOC,H,	Ethanol	617, 148
	(C.11.).C110SO.C.11.C11n	(C,11;),CIIC(C,H;)(CO,C,II;),	Poor	Na .	C,H,	238
	(0,11,0,0110],00	(C,H,),C11C(C,H,)(C0,C,H,),	35	KOCH(C2H5),	[(C2H5)2CHO]2CO	890, 330
	C.II.CII(CII.)CII.Br	C, H, CII(CII,)CII, C(C, II,)(CO, C, II,)	30	NaOC2H5	Ethanol	148
	C.II.C(CII.), Ilt	C,11,C(C11,),C(C,11,)(C0,C,H,),	ıG	NaOC,H,	Ethanol	15
	CH,CH = CHCH(CH,)X;	cit, CH = CitCH(CH,)C(C, H,S)(CO,C,H,S)2	1	NaOC <sub>2</sub> H <sub>s</sub>	Ethanol	547
	(CII,),C=CHCH,Br	$(CH_3), C = CHCH, C(C, H_3)(CO_2C, H_3)_2$	62	Na0C2H5	Ethanol	557
	n-C,II,OCII,CI	$n$ - $C_1$ 11,0C1 $F_2$ C( $C_2$ 1 $F_3$ )( $\tilde{C}$ O <sub>2</sub> C <sub>2</sub> 1 $F_3$ )2	20	Na	Ether	542
	i-c,11,0c11,c1	i-C,II,0CII2C(C,II,)(CO,C,II,)2	99	Na	Ether	543
	ກ-ຕຸ້ນກຸດຕາໃຕນ,ຕ	n.C, II, OCII(CH, )C(C, II, )(CO, C, II, )2	62	NaNII,	C,II,-ether	203
	(CII, 3), COCII, CI	(C113),COC11,C(C,115)(CO,C,H5),	1	NaOC <sub>2</sub> II <sub>5</sub>	Toluene	125
	n-C4II,SCIII,CI	n-C, II, SCII, C(C, II, )(CO, C, II, s),	1	NaOC2H5	Toluene	125
	Callsch(cha)schzel	C211,C11(C113)SC11,C(C2H5)(CO2C2H5)2	1	NaOC2H5	Toluene	125,893
	¿cinsenici	i-C,11,5C112C(C,115)(CO2C,115)2	1	Na0C,11,	Tolucne	125
	C,11,5C11,C11(C113)C1	C2NSCH2CH(CH3)C(C2H5)(CO2C2NS)2	70-75	NaOC2H5	Toluene	554
	CII,CIIBrCO,C,III,	C211502CC11(CH3)C(C2H5)(CO2C2115)2	1	Na	None	162
	CII3CIII3cCO2C2II3	C211,02CC11(C113)C(C2115)(CO2C2113)2	30	NaOC2II5	Ethanol	223
	I(C11 <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> 11 <sub>5</sub>	$C_2H_5O_2^*C(CH_2)_2C(C_2H_5)(CO_2C_2H_5)_2$	1	Na	Ether	804
	1(C11 <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub>	$C_2\Pi_5O_2C(C\Pi_2)_2C(C_2\Pi_5)(CO_2C_2\Pi_5)_2$	١	Na	C,H,	804
	Cyclobutylmethyl tosylate	Diethyl ethyl(cyclobutylmethyl)malonate	65	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	334
	Cyelopentyl bromlde	Diethyl ethyl(eyelopentyl)malonate	1	Na	Toluene	800
	Cyclopentyl bromlde	Diethyl ethyl(eyelopentyl)malonate	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	617
	Tetrallydrofurfuryl bromide	Diethyl ethyl(tetrahydrofurfuryl)malonate	1	NaOC, II,	Ethanol	543
	2-Chlorotetrahydropyran	Diethyl ethyl-(2-tetrallydropyranyl)-	1	Nali	Toluene	683
		maionate				
	z-Chloromethylthlophene	Diethyl ethyl-(2-thenyl)malonate	}	Na	None	897
	z-Methyl-4-thloro-	Dlefthyl efflyf-(2-methyl-4-thiazolyl-	20	NaOC <sub>2</sub> II <sub>5</sub>	Ethanol	548
	C.	methyl)maionate				
	- 1 L					
	n-Cellight	n-C <sub>6</sub> II <sub>13</sub> C(C <sub>2</sub> II <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub>	£9	$NnOC_2H_5$	Ethanol	538
	n-C311,CII(C311,)X;	n-C <sub>4</sub> 11,5CH(C113)C(C <sub>2</sub> 11,5)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>4</sub> 11,CH(C <sub>4</sub> 11,5C(C <sub>4</sub> H <sub>5</sub> )CO <sub>2</sub> C <sub>4</sub> H <sub>5</sub> ).	1 1	NaOC <sub>2</sub> II <sub>5</sub>	Ethanol	617
Note: References	Note: References 577-1080 are on up. 322-331	7.5. 2.7. 2.7. 2.7. 2.7. 2.7. 2.7. 2.7.		114002115	lounna	547
• The disoantyl est	• The discount before was used in this executions					

• • The discount ester was used in this experiment.

† The halogen was not specified.

# TABLE III-Continued

Alentation of Monoagenelamonic Esters,  $\mathrm{RCH}(\mathrm{CO}_2\mathrm{R})_2$ (The diethyl ester was used unless otherwise indicated.)

		T. Lat.			Refer-
Alky Ixting	•	11CH1	Base	Solvent	ence
Agent.		a ;	11 00 11	Rehand	148,550
n.C <sub>2</sub> 11,C11(C11 <sub>2</sub> )C11 <sub>2</sub> 11c	n.c.11,CUCH5PCH2CC24H3XCO2C2H5)2 n.c.11,CUC-H3XCO3C4H322	33-13	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	Kthanol	718,550
31,61119,1-1			11 200%	Ethanol	550
att the transfer of	(C,11,),C11('11,'V(',11,')('C0,'C,11,'))	l	MIOC 115	Thona	550
3[[("][,))], (",",")	1.C, 11, C11(C113)C(C113)(CO2C2113)3	1:	NaOC2115	Ethanol	060
21. ( 1.77.) ( 1.77.)	(C11,), C(C11,), C(C4,11,)(CO <sub>2</sub> C4,11 <sub>3</sub> ) <sub>2</sub>		230C 2115	131100001	547
((1111)) ((1111))		1	NaOC;1115	Common	900
* V. (2.11.2. ) [1.1.2. ] [1.1.2. ] [1.1.2. ]		1	NaOC <sub>2</sub> II <sub>5</sub>	Ethanol	010
(113. (((113)(11((113)))		i	ı	1	17.4
10,411,010,111,011		3.6	NaNII.	C,ll, ether	503
11.C. 11.0.C.1((C.11 <sub>2</sub> )(T	3.(',11,0C11(C11,3)('(',211,5)('C')',',1'',5/3	: 1	NaOC.11	Toluche	125
D. 11.18.11.13.11	n-C <sub>2</sub> 11 <sub>11</sub> 5C11 <sub>2</sub> C(C <sub>2</sub> 115ACO <sub>2</sub> C <sub>2</sub> 11 <sub>3</sub> 7 <sub>2</sub>	. 1	NoOC.11.	Toluene	125
15,117,8(11,7)	1.C.11, SCII. ((C.11.5)(CO.1.5)2		V.00.11.	Tohene	125
n.c.11,CB(CH13)SCH2CH	11.C.11.C.11(C.11.1)SC.11.1.C.(C.1.11.1)(C.O.3.1.2.11.2).2	l	Stringer		
12 1 210000 20 00		70-00	NaOC, II,	Loinene	100
1.5(811))(011))(±	"C IT SCHOOL DOOR ("IL")"	20-90	NaOC, II,	Toluene	120,809
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		30-10	NaOC, II,	Toluene	126
(1112×C11(C11111-1)C1		30-10	Na0C, 11,	Tolucue	120,890
12(1,11,2)1122,111,2		20-10	NaOC.II.	Toluene	126,899
12(*11*20110*11*10*1		25	N. C.	None	162
C. H. C'H Br C'O, C, 18,	C*11*0*CC11(C*11*0)C(C*11*0)*C*11*0	1	10 to	Tithened	500
C.11.C11111.CO.C.11.	C,11,0,CCH(C,11,)C(C,11,)(CO,C,11,)	53	NaUC2115	Emanor	60.
COLUMN CHECO. C. II.	C.11, 0, CC(C11,), C(C,11,)(CO,C,11,),	ı	Na	None	701
11.2.3.0.3.1.3.1.1.1.1.2.1.1.1.2.1.1.1.1.1.1.1.1	C.11.0.CCC11.3.CCC.11.3(CO.C.11.3)	얽	NaOC <sub>2</sub> 11 <sub>5</sub>	Ethanol	27.7
13 113 (COV ( 11 0)	(C.11.2). SCOCII. (C.C.11.2).	1	NaOC <sub>2</sub> III <sub>5</sub>	Ethanol	530
Cyclopentylinethyl tosylato		00	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	33 <del>4</del>
បំ					
(n.C.115)2CHBr	$(n-c_2\Pi_1)_2$ CHC $(C_3\Pi_3)(CO_3C_3\Pi_3)_2$	31	NaOC <sub>2</sub> II <sub>5</sub>	Ethanol	148, 550 617
can cucatomical (cutable	1) Br C, H, CH(CH, ) CH(CH, ) C(C, H, )(CO, C, H, ),	1.1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanof Ethanof	550 550
t-C <sub>4</sub> H <sub>4</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> Br	1.C.11.0CH1.CH1.CC.11.3CC.11.2.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.1.	1	Na0C2112	Ethanol	550

203 125, 893 553 126 126	125 125 126 126 223 777 725 334	890, 330 740 900 125, 890	769 901 901 901 550 550	374 126 902 663
C <sub>6</sub> H <sub>6</sub> -ether Toluene Toluene Toluene Toluene	Louene Toluene Toluene Ethanol Ethanol Ethanol Ethanol	(C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> O) <sub>2</sub> CO Ethanol Ethanol Toluene	Ether Ethanol Ethanol Ethanol Ethanol Ethanol	Toluene Ethanol (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO
NaNE, NaOC2H, NaOC2H, NaOC2H, NaOC2H,	NAOC,2H, NAOC,2H, NAOC,2H, NAOC,2H, NAOC,2H, NAOC,2H, NAOC,2H,	NaOCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>6</sub> NaOC <sub>2</sub> H <sub>5</sub>	Na NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	
71 70-90 70-90 70-90	70-90 70-75 30-40 Poor ——————————————————————————————————	52   54	85 41 43 1	30-40
i.C <sub>5</sub> H <sub>11</sub> OCH(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n·C <sub>8</sub> H <sub>13</sub> SCH <sub>2</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> n·C <sub>8</sub> H <sub>11</sub> SCH(CH <sub>3</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> n·C <sub>8</sub> H <sub>11</sub> SCH(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> i·C <sub>3</sub> H <sub>11</sub> SCH(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>3</sub> )(CC <sub>3</sub> H <sub>3</sub> )(CC <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> i·C <sub>3</sub> H <sub>11</sub> SCH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>3</sub> )(CC <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> i·C <sub>3</sub> H <sub>11</sub> SCH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>3</sub> )(CC <sub>3</sub> H <sub>3</sub> ) <sub>3</sub>	c <sub>2</sub> H <sub>5</sub> CH(C <sub>2</sub> H <sub>5</sub> )CH <sub>2</sub> SCH <sub>2</sub> CCH <sub>2</sub> M(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) n-C <sub>3</sub> H <sub>7</sub> GH(C <sub>4</sub> H <sub>5</sub> )CGC <sub>4</sub> H <sub>5</sub> MCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>4</sub> H <sub>5</sub> SCH <sub>2</sub> CH(GH <sub>3</sub> )CC <sub>2</sub> H <sub>5</sub> MCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>4</sub> H <sub>5</sub> SCH(C <sub>4</sub> H <sub>5</sub> )CC <sub>2</sub> H <sub>5</sub> MCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH(C <sub>3</sub> H <sub>7</sub> +)CC <sub>2</sub> H <sub>5</sub> MCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH(C <sub>3</sub> H <sub>7</sub> +)CC <sub>2</sub> C <sub>4</sub> H <sub>5</sub> MCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCCC <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCCC <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Dichyl chly-[β-(2-cyclopentyrlthyl)malonate Dichyl chly-[β-(2-cyclopentenyl)chlyl]- malonate	C <sub>6</sub> H <sub>2</sub> CH <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> )(CO <sub>6</sub> C,H <sub>5</sub> ) <sub>2</sub> p-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> p-IC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyl ethyl[(eyelohexylthio)methyl]- malonate	n-C <sub>8</sub> H <sub>1</sub> ,C(C <sub>2</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> (+)-n-C <sub>6</sub> H <sub>1</sub> ,OH(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> (-)-n-C <sub>6</sub> H <sub>1</sub> ,OH(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> (+ -)-n-C <sub>6</sub> H <sub>1</sub> ,OH(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>3</sub> H <sub>1</sub> ,CH(CH <sub>3</sub> )(CH <sub>2</sub> ) <sub>3</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>4</sub> H <sub>2</sub> CH(C <sub>3</sub> H <sub>3</sub> )C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>3</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> (CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	n-C <sub>1</sub> H <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>3</sub> ) <sub>3</sub> C(C <sub>3</sub> H <sub>3</sub> ) <sub></sub>
i-C <sub>3</sub> H <sub>11</sub> OCH(CH <sub>3</sub> )Cl n-C <sub>3</sub> H <sub>13</sub> SCH <sub>2</sub> Cl n-C <sub>3</sub> H <sub>11</sub> SCH <sub>2</sub> Cl n-C <sub>3</sub> H <sub>11</sub> SCH(CH <sub>3</sub> )Cl i-C <sub>3</sub> H <sub>11</sub> SCH(CH <sub>3</sub> )Cl	C <sub>2</sub> U <sub>3</sub> CH(C <sub>2</sub> H <sub>2</sub> )CH <sub>2</sub> SCH <sub>2</sub> CI n-C <sub>3</sub> H <sub>2</sub> CH(C <sub>4</sub> H <sub>2</sub> )CCH <sub>2</sub> )CI n-C <sub>4</sub> H <sub>3</sub> CH(C <sub>4</sub> H <sub>2</sub> )CI n-C <sub>4</sub> H <sub>3</sub> CH(C <sub>2</sub> H <sub>3</sub> )CI i-C <sub>4</sub> H <sub>4</sub> CHBrCO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> C <sub>3</sub> H <sub>4</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> I CHCl(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ) p-Cyclopentylethyl bromide p-Cyclopentenyl)ethyl hromide	(C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> O <sub>3</sub> CO p-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Cl p-IC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Dr Chloromethyl eyeloliexyl sulfide	C <sub>8</sub> n·C <sub>8</sub> H <sub>17</sub> Br (+)·n·C <sub>9</sub> H <sub>13</sub> CH(CH <sub>3</sub> )Br (-)·n·C <sub>9</sub> H <sub>13</sub> CH(CH <sub>3</sub> )Br (+)·n·C <sub>9</sub> H <sub>13</sub> CH(CH <sub>3</sub> )Br (+)·n·C <sub>9</sub> H <sub>15</sub> CH(CH <sub>3</sub> )Br n·C <sub>3</sub> H <sub>2</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> J <sub>3</sub> Br n·C <sub>4</sub> H <sub>9</sub> CH(C <sub>1</sub> J <sub>3</sub> )CH <sub>2</sub> J <sub>3</sub> Br (CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> CH (CH <sub>3</sub> )CH <sub>2</sub> CH (CH <sub>3</sub> )CH <sub>2</sub> Br	n-C <sub>1</sub> H <sub>2</sub> Q(CH <sub>2</sub> ) <sub>2</sub> Q(CH <sub>2</sub> ) <sub>2</sub> Br (C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> CHCH(SC <sub>2</sub> H <sub>3</sub> )Cl β-Cyclohexylethyl bromide β-Cyclohexylidene¢thyl bromide

Note: References 577-1080 are on pp. 322-331.  $\updownarrow$  The halogen was not specified.

# TABLE III—Continued

Alkylation of Monoalkylmalonic Estens,  $R'CH(CO_2R)_2$  (The diethyl ester was used unless otherwise indicated.)

reier-	ence 881	374 205 374	003 542 891	891 904, 894 894	100	11	250	550 900 371	906 908
	Solvent	Ether	Toluene Ether	Cane Cane Cana	Ethanol	Ethanol	Ethannl	Ethanol Ethanol	Ethanol Ethanol
	Base	Na l	NaOC, II,	K K K K K k	NaOC <sub>2</sub> II <sub>5</sub>	Na0C <sub>2</sub> II <sub>3</sub>	NaOC <sub>2</sub> H <sub>3</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>6</sub>	NaOG <sub>1</sub> 11 <sub>5</sub> NaOG <sub>1</sub> 11 <sub>5</sub>
Trivia.	* 10m*	2   2 2   3	118	1111	1	<b>SO</b>	1	181	١ಪ
•	Product	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> )2(C <sub>4</sub> H <sub>5</sub> )7 C <sub>6</sub> H <sub>5</sub> O(CH <sub>2</sub> )2(C <sub>2</sub> H <sub>3</sub> )7 C <sub>4</sub> H <sub>5</sub> O <sub>1</sub> CH <sub>2</sub> (C <sub>2</sub> H <sub>2</sub> )1 C <sub>4</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> (C <sub>3</sub> H <sub>5</sub> )1	Calconsolves	C,H,COCH,C(C,H,NCO,C,H,N,C,H,CO,C,H,N,CO,C,H,N,CO,C,H,N,CO,C,H,N,CO,C,H,N,CO,C,H,N,CO,C,C,H,N,CO,C,H,N,C,C,H,N	11,50,000 11,500	HCC(C_1U_5)CO_1C_1U_5 H_CO_HCU_1C(C_2U_5)CO_2C_2U_5	0C n-C_H_CH(CH_)CH(C,H_)CH_C(C_2H_)-	(CO <sub>1</sub> C <sub>2</sub> H <sub>3</sub> ), i-C <sub>2</sub> H <sub>11</sub> CH(C <sub>2</sub> H <sub>3</sub> )CH <sub>2</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ), C <sub>2</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ), C <sub>3</sub> H <sub>3</sub> O(CH <sub>2</sub> ) <sub>3</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ),	Dictiyl cthyl-(6-cyclohexylbutyl)malonate Dictiyl cthyl-(5-methoxy-2,4- dimethylbenzyl)malonato
	Alkylatiog Agent	$C_6H_5(CH_2)_2Dr$ $C_6H_5O(CH_2)_2Cl$	C,H,CH,SCH,CH C,H,CH(CH,J)X; p-CH3,OC,H,CH,O	Censocnsci Cansocnsci Cansocnsci Cansocnsci	C,U,COCH,Br C,U,COCH,Br	HsG6CH-CH2	0.	Control of the Contro	C <sub>10</sub> 2-Cyclohexylbutyl bromide 5-Methoxy-2,4-dimethyl- benzyl ellioride-KI

R' $C_2H_5$  (Cont.)

	thiazolo  C <sub>11</sub> n-C <sub>11</sub> L <sub>13</sub> X‡  1-Bromomethylnaphthaleno 2-Bromomethylnaphthaleno  C <sub>12</sub> n-C <sub>12</sub> L <sub>12</sub> X‡  h-Cr-t-Butylphenyllethyl- bromide 1-Aeenaphthenyl ehloride  C <sub>13</sub> -C <sub>16</sub> n-C <sub>13</sub> H <sub>27</sub> Br  n-C <sub>14</sub> H <sub>23</sub> I  n-C <sub>14</sub> H <sub>23</sub> I  n-C <sub>16</sub> H <sub>23</sub> I  c <sub>16</sub> C <sub>17</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>17</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>17</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>17</sub> C <sub>16</sub> C <sub>16</sub> C <sub>16</sub> C <sub>17</sub> C <sub>16</sub> C <sub>18</sub>	thlazolylmethyl)malonate  n-C <sub>11</sub> H <sub>22</sub> C(C <sub>2</sub> H <sub>5</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> Diethyl ethyl-(1-maphithylmethyl)malonato  Diethyl ethyl-(2-naphithylmethyl)malonato  n-C <sub>12</sub> H <sub>35</sub> C(C <sub>2</sub> H <sub>5</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> Diethyl ethyl-(β-(p-t-butylphenyl)ethyl)-  malonate  Diethyl ethyl-(1-acenaphthenyl)malonate  n-C <sub>13</sub> HC <sub>27</sub> (C <sub>2</sub> H <sub>5</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> n-C <sub>13</sub> HC <sub>27</sub> (C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> n-C <sub>14</sub> HC <sub>23</sub> (C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> n-C <sub>16</sub> HC <sub>33</sub> (C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> n-C <sub>16</sub> HC <sub>33</sub> (C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> n-C <sub>16</sub> HC <sub>33</sub> (C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> n-C <sub>16</sub> HC <sub>33</sub> (C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> n-C <sub>16</sub> HC <sub>33</sub> (C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup> n-C <sub>16</sub> HC <sub>33</sub> (C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sup>2</sup>	10 0 10   E 2 2 E 8	NaOC <sub>2</sub> II <sub>5</sub> Na Na NaOC <sub>2</sub> II <sub>5</sub>	Ethanol C <sub>6</sub> H <sub>6</sub> C <sub>6</sub> H <sub>6</sub> C <sub>6</sub> H <sub>6</sub> Ethanol Toluene Ethanol	887 153 153 153 413 413 824 887 887 887 606 135
<del>‡</del>	n-C10II31Br	$(^{\mathrm{CH}_{2})_{2}}\mathrm{C}(C_{1_{0}}\mathrm{H}_{21}\cdot n)\mathrm{CO}_{2}C_{2}\mathrm{H}_{5}$	ı	NnOC <sub>2</sub> II <sub>5</sub>	Ellanol	527
	$n$ - $C_{12}H_{23}Br$	0	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	525
	n-('12 II'37 Br	0	1	NaOC, II.	Ethanol	1
		\$11.53.603(11.48.11)\dots \dots \dot	1	,		MTR)
Wee References 375-1480 and The Indoor was not specified. If The Latence Clifter Clifter of the Colors of the Clifter of the C	o on pp. 822-331. By was used as the eater	. to be alkylated,		\$11 <b>8</b>	Ethanol	ta a

TABLE III—Continued

ALKYLATION OF MONOALKYLMALONIC ESTERS, R'CH(CO<sub>2</sub>R)<sub>2</sub>

,	.ence ence 527	907 908 908	908	900	204	931	555	172
	Solvent Ethanol	Ethanol Ethanol Tolunc-cthanol	Tolurne-ethanol	Ethanol Toluene-ethanol	Ethanol Ethanol	Ethanol Ether	C <sub>e</sub> II <sub>e</sub>	Ethanol
(moore)	Base NaOC <sub>2</sub> II <sub>5</sub>	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	Na0C <sub>2</sub> 11 <sub>5</sub>	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC2H 5 Na	Na	NaOC <sub>2</sub> U <sub>5</sub>
50 marc	Yield,	111	1	1.1	18	1 1	i	1
(The diethyl ester was used unless otherwise mucrecut)	Product (CH <sub>3</sub> ) <sub>2</sub> C(C <sub>16</sub> H <sub>32</sub> <sup>n</sup> )CO <sub>2</sub> C <sub>4</sub> H <sub>5</sub> 	CH <sub>3</sub> = CHCH <sub>4</sub> C(OC <sub>2</sub> H <sub>3</sub> )(Co <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> i-C <sub>1</sub> H <sub>2</sub> CH = CHCH <sub>3</sub> C(Oc <sub>2</sub> H <sub>3</sub> )(Co <sub>2</sub> G <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> In(CH <sub>2</sub> ) <sub>2</sub> C(OC <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> G <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> and (C <sub>1</sub> H <sub>3</sub> O <sub>2</sub> C(Oc <sub>2</sub> H <sub>3</sub> )(CH <sub>3</sub> ) <sub>2</sub> .	C(OC,11,3/CO <sub>2</sub> C <sub>3</sub> H3)3 Dr(CH2,4,CCOC,11,3/CO <sub>2</sub> C <sub>3</sub> H3)2 and (C <sub>3</sub> H3O <sub>2</sub> O)2C(OC <sub>3</sub> H3)(CH <sub>2</sub> )4-	C(OC,II,)(CO,C,II,), C(II,CII,)(CO,C,II,), IC(II,),C(OC,II,)(COC,II,)(CO,C,II,), IC(II,),C(OC,II,)(CO,C,II,),COC,II,),COC,II,)	$ \begin{array}{l} (\ddot{\mathrm{CO}}_{1}\dot{\mathrm{L}}_{1}^{1}\mathrm{L}_{1}^{3})\\ \mathrm{CH}_{2}=\mathrm{CH}(\mathrm{CH}_{1}^{3})_{\mathrm{C}}(\mathrm{CO}_{2}\mathrm{H}_{3})(\mathrm{CO}_{2}\mathrm{G}_{3}\mathrm{H}_{2})\\ (\dot{\mathrm{C}}_{2}\mathrm{H}_{3}\mathrm{O}_{2}\mathrm{C})_{\mathrm{C}}(\mathrm{CH}_{3})\mathrm{CH}_{2}\mathrm{C}(\mathrm{CH}_{3})(\mathrm{CO}_{2}\mathrm{C}_{3}\mathrm{H}_{3})\\ \end{array} $	n-c <sub>3</sub> H <sub>2</sub> C(CH <sub>3</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> CH(C(c <sub>3</sub> H <sub>2</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> and (C <sub>3</sub> H <sub>3</sub> O <sub>2</sub> C) <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> -n)CHCl <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub>	$(CII_2)_2C(G_3II_7\cdot n)CO_2G_3II_3$	OCO Br(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub>
	Alkylating Agent n-C <sub>16</sub> H <sub>33</sub> Br	$C_3 - C_{11}$ $CH_2 = CHCH_2Dr$ $i \cdot C_i H_i CH = CHCH_2Dr$ $Br(CH_2)_3 Dr$	Br(CII <sub>2</sub> ) <sub>4</sub> Br	$C_6II_5CII = CIICH_2Bt$ $Br(CH_2)_{10}Bt$	$CH_2 = C\Pi(CH_2)_9 Br$ $CH_3 I$	Ci CH <sub>2</sub> I CHCi <sub>3</sub>	$C_{3}$ $\mathrm{Br}(\mathrm{CH}_{2})_{2}\mathrm{Br}$	Br(CH <sub>3</sub> ) <sub>3</sub> Br
	R' †† (Cont.)	$c_2 H_5 O$			сп,осп,	$C_3$ $n$ - $C_3$ H $_7$	<del>+-</del>	$n$ - $C_3H_7$

CH <sub>2</sub> —CH <sub>2</sub>	$(\mathrm{CH}_2)_2\mathrm{CH}(\mathbf{C_3H_2\cdot n})$ $\begin{vmatrix} & & & & & & & & & & & & \\ & & & & & & $	70	$NaOC_2H_5$	Ethanol	282
C, B, SOH, CI C, B, SOH, CI OH, SOH(OH, OI Br(CH, ), Br	C <sub>2</sub> H <sub>3</sub> SCH <sub>2</sub> CC <sub>3</sub> H <sub>7</sub> -n\CO <sub>4</sub> C <sub>2</sub> H <sub>3</sub> \) <sub>2</sub> CH <sub>3</sub> SCH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> -n\(CO <sub>4</sub> C <sub>2</sub> H <sub>3</sub> \) <sub>2</sub> In\(CH <sub>2</sub> \) <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> -n\(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> \) <sub>2</sub>	70-00	$NaOC_2H_5$ $NaOC_2H_5$ $Na$	Toluene Toluene	125 126 656
C4 C3H,CUICH3,Br C3H,OCCH3,Br C3H,OCCH3,Br C4H,GCH(CH3,2CI C4H,SCH(CH3,2CI C3H,SCH(CH3,1CI C1CH2,CO2,C2H3,CI C1CH2,CO2,C2H3,CI C1CH2,CO2,C2H3,CI C1CH2,CO2,C2H3,CI	C <sub>2</sub> H <sub>3</sub> CH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> ·n)(CO <sub>3</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>3</sub> OC(CH <sub>3</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>3</sub> OCH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>3</sub> SOH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	53 43 66 40-50 70-90	NAOC <sub>2</sub> H <sub>5</sub> NAOC <sub>2</sub> H <sub>5</sub> NAON <sub>2</sub> NAOC <sub>2</sub> H <sub>5</sub> NA	Ethanol Ethanol C <sub>6</sub> H <sub>6</sub> -ether Ethanol Toluene Ether C <sub>6</sub> H <sub>6</sub>	909, 547 910 203 541 126 653
C <sub>5</sub> n-C <sub>5</sub> H <sub>11</sub> Br n-C <sub>5</sub> H <sub>5</sub> SCH <sub>2</sub> Ct C <sub>2</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> Br i-C <sub>5</sub> H <sub>41</sub> Dr i-C <sub>5</sub> H <sub>5</sub> CH(CH <sub>3</sub> )Ct CH <sub>3</sub> CH(CH <sub>3</sub> )Ct CH <sub>3</sub> CHBrCO <sub>5</sub> C <sub>2</sub> H <sub>5</sub> Cyclopentyl halide‡	n-C <sub>2</sub> H <sub>11</sub> C(C <sub>2</sub> II <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> ) <sub>2</sub> n-C <sub>4</sub> H <sub>2</sub> CH <sub>2</sub> C(C <sub>3</sub> II <sub>7</sub> -n)(CO <sub>2</sub> C <sub>4</sub> H <sub>2</sub> ) <sub>2</sub> C <sub>2</sub> II <sub>3</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> C(C <sub>3</sub> II <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> i-C <sub>3</sub> H <sub>11</sub> C(C <sub>3</sub> II <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> i-C <sub>3</sub> H <sub>1</sub> C(C <sub>3</sub> II <sub>7</sub> -n)(CO <sub>2</sub> C <sub>3</sub> II <sub>3</sub> ) <sub>2</sub> C <sub>3</sub> H <sub>2</sub> COI(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>3</sub> O <sub>3</sub> CCII(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub> ) <sub>2</sub> Diethyl cyclopentyl-(n-propyl)malonate	73   1   41   70–90   25	NAOC2H5 NAOC2H5 NAOC2H5 NAOC2H5 NAOC2H5 NAOC2H5	(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO Toluene Ethanol Ethanol Toluene Ethanol	44 125 551 718, 748 120 223
C <sub>0</sub> n-C <sub>1</sub> H <sub>3</sub> SCH(CH <sub>3</sub> )CI  C <sub>4</sub> H <sub>5</sub> CHRCO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> (CH <sub>3</sub> ) <sub>2</sub> CHCO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> 2.4-Dinitrechlorobenkene	n-C <sub>4</sub> H <sub>5</sub> SCH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>3</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>3</sub> CCH(C <sub>2</sub> H <sub>5</sub> )c(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>4</sub> H <sub>5</sub> O <sub>2</sub> CC(CH <sub>3</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> Diethyi n-propyi-(2,4-dialtrophenyl)- malomate	70–90 12 21 54	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> Na	Toluene Ethanol Ethanol	126 223 223 139

More References 577-1080 are on pp. 322-831,

† The halogen was not specified,

† The lactone CH<sub>2</sub>CH<sub>2</sub>CHCO<sub>4</sub>C<sub>4</sub>H<sub>3</sub> was used as the ester to be alkylated.

TABLE III—Continued

Alexiation of Monoalkylmalonic Esters, R'CH(CO<sub>2</sub>R)<sub>2</sub>

(The diethyl ester was used unless otherwise indicated.)

	(The d	(The diethyl ester was used unless otherwise mulcaucu.)	amiii es	anca-)		
	Alkylating Agent	Product	Yield,	Baso	Solvent	Refer- ence
cont.)	C <sub>7</sub> i·C <sub>3</sub> H,CHBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> β·Cyclopentylethyl bromide	C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH(C <sub>2</sub> H <sub>2</sub> -i)C(C <sub>3</sub> H <sub>7</sub> -n)COO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> ) <sub>2</sub> Diethyl n-propyl-(β-cyclopentylethyl)- malonate	Poor 50-60	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ethanol Ethanol	755
	$c_{ m s}$ ho-Cyclohexylethyl bronide	Diethyl $n$ -propyl- $(\beta$ -cyclohexylethyl)-	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	506
	$C_6H_5O(CH_2)_2$ Br	malonate C <sub>6</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	8	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	910
	$G_{m s}$ $\gamma$ -Cyclohexylpropyl bromide	Diethyl n-propyl-(p-cyclohexylpropyl).	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	506
	C6H5O(CH2)2CI	malonate C <sub>6</sub> H50(CH2)2C(C3H7-11)(CO2C2H5)2	23	Na0C <sub>3</sub> H <sub>7</sub> ·n	n.C₃11;OII	*** t- i>
	$C_{10}$ $n\text{-}C_{10}\mathrm{H}_{21}\mathrm{X}_{\circ}^{\star}$ $\delta\text{-}Cyelohexy:lbutyl bromide}$	$n \cdot C_{10} \Pi_{21} C(C_2 \Pi_7 \cdot n) CO_2 C_2 \Pi_5)_3$ Djetnyl $n \cdot propyl \cdot (\theta \cdot cyclohexylbutyl) \cdot malomate$	1.1	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	Ethanol Ethanol	S87 902
	C <sub>11</sub> -C <sub>16</sub> n-C <sub>11</sub> H <sub>21</sub> X; n-C <sub>11</sub> H <sub>22</sub> X; p-(1-Naphthyl)ethyl bromide	n-C <sub>11</sub> H <sub>13</sub> C(C <sub>2</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>12</sub> H <sub>22</sub> C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Diethyl n-propyl-[f-(1-napluthyl)cthyl]-	118	NaOC <sub>2</sub> 11 <sub>5</sub> NaOC <sub>2</sub> 11 <sub>5</sub> K	Ethanol Ethanol C <sub>6</sub> II <sub>6</sub>	888 887 419
	n-C <sub>13</sub> H <sub>27</sub> X <sup>*</sup> ; n-C <sub>14</sub> H <sub>29</sub> X <sup>*</sup> ; n-C <sub>16</sub> H <sub>33</sub> I None None	nnlonar n-C <sub>11</sub> H <sub>2</sub> :Q(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>11</sub> H <sub>2</sub> ·Q(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>14</sub> H <sub>3</sub> ·Q(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>2</sub> ) <sub>2</sub> n-C <sub>14</sub> H <sub>3</sub> ·Q(C <sub>3</sub> H <sub>1</sub> -n)(CO <sub>2</sub> C <sub>3</sub> H <sub>2</sub> ) <sub>2</sub> Diethyl cyclobutane-1,1-dicarboxylate	1 1 88 87 7	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>3</sub> H <sub>5</sub> NaOC <sub>3</sub> H <sub>5</sub>	Ethanol Ethanol Ethanol Ethanol	883 887 135 622, 480, 490

92	527	627	569	145	890 35 204 172	536 205 125 52 44 56	536, 770 44 44 125
Ether Toluene	Ethanol	Ethanol	Ethanol	Ethanol	(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO t-C <sub>4</sub> H <sub>9</sub> OH Ether Ethanol	Ethanol Ether Toluene Ether (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO Ethanol	Ethanol (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO Toluene
Na(C,H,CHCN) Na[C,H,c-	NaOC <sub>2</sub> H <sub>5</sub> /21	$ m NaOC_2H_5$	NaOC <sub>2</sub> H <sub>S</sub>	NaOC2H5	$egin{array}{ll} egin{array}{ll} egi$	NaOC2H5 Na NaOC2H5 Na NaOC2H5 MG(OC2H2)2	NaOC2H5 NaOC2H6 NaOC2H5 NaOC2H5
11	1	1	1	Very	52811	ca. 80 33 40 84 90	ca. 80 26 67
Dictiyl cyclobutane-1,1-dicarboxylate Dlettyl cyclobutane-1,1-dicarboxylate	CH3CHCH2C(C14H2n-n)CO2C2H5	CH3CHCIL.C(C16H337")CO2.C2H5	C3H,C(CH3)(CO2C2H5)2	$i \cdot c_3 \Pi_7 \mathrm{C}(C_2 H_5) (\mathrm{CO}_2 \mathrm{C}_2 \Pi_6)_2$	C.JL,C(C2H,)(CO,C2H,), i-C.JL,C(C2H,)(CO,C2H,), CH,OCH,C(C,H-i)(CO,C2H,), Br(CH <sub>2</sub> ),C(C,JL-i)(CO,C2H,);	$\begin{array}{ll} n.C_3H_1C(C_3H_1^{-4})(CO_2C_2H_3)_2\\ C_2H_3CCH_2C(C_3H_1^{-4})(CO_2C_2H_3)_2\\ C_2H_3CCH_2C(C_3H_1^{-4})(CO_2C_2H_3)_2\\ (4\cdot C_3H_1)_2C(CO_2C_3H_3)_2\\ CH_3=CHCH_2C(C_3H_1^{-4})(CO_2C_2H_3)_2\\ CH_2=CHCH_2C(C_3H_1^{-4})(CO_2C_2H_3)_2\\ CH_2=CHCH_2C(C_3H_1^{-4})(CO_2C_2H_3)_2\\ \end{array}$	n-c,H,G(c,H,-i)(C0,C,H,), C,H,GH(CH,)Q(C,H,-i)(C0,C,H,), i-C,H,G(C,H,-i)(C0,C,H,), i-C,H,SGH,G(C,H,-i)(C0,C,H,),
None None	$n$ - $C_{14}H_{29}Br$	n-C <sub>10</sub> H33Br	$G_1$ $CH_3I$	G₂ G₂H₅X‡	(C <sub>2</sub> H <sub>3</sub> O) <sub>2</sub> CO C <sub>2</sub> H <sub>3</sub> N; CH <sub>3</sub> OCH <sub>2</sub> Cl Br(CH <sub>2</sub> ) <sub>2</sub> Br	$C_3$ $n \sim C_3H_2$ Dr $C_2H_3 > C_1H_2$ Cr $C_2H_3 > C_1H_3$ Cr $C_3H_3$ Cr $C_3H_3$ Cr $C_3H_3$ Cr $C_3H_2$ Cr $C_3$	C4 n-C <sub>4</sub> H <sub>2</sub> Br C <sub>2</sub> H <sub>2</sub> CH(CH <sub>3</sub> )Br i-C <sub>4</sub> H <sub>3</sub> Br i-C <sub>3</sub> H <sub>3</sub> SCH <sub>2</sub> Cl
$I(CH_2)_3$	4 4	#	$i\text{-}\mathrm{C}_{3}\Pi_{r}$				

Note: References 577-1030 are on pp. 322-331. ‡ The halogen was not specified. †† The lactone CH<sub>3</sub>CHCH<sub>2</sub>CHCO<sub>2</sub>C<sub>2</sub>H<sub>5</sub> was used as the ester to be alkylated.

TABLE III—Continued

Alkylation of Monoalkylmalonic Esters,  $R'CH(CO_2R)_2$ 

	Refer- Solvent ence		Ethanol 223 Ethanol 725	Ethanol 902	Ethanol 910	Ethanol 902	n.C <sub>2</sub> II,01I	Ethanol 887 Ethanol 902	Ethanol 888 Ethanol 897 C <sub>4</sub> H <sub>6</sub> 419	Ethanol 888 Ethanol 857 Ethanol 135 Ethanol 622, 180, 400 Ethanol 315
icated.)			NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	NaOC2H3 E	NaOC2IIs Et	NaOC <sub>2</sub> II <sub>5</sub> Et	NaOC <sub>3</sub> H <sub>7</sub> -n n-'	NaOC,H, Ed NaOC,H, Ed	NaOC,H, ES NaOC,H, ES K	NnOC2H3  NnOC2H3  NaOC2H3  NnOC2H3  NnOC2H3  NnOC2H3
rwise indi	Yield,	?	12 Poor 50-60	1	33	I	52	1.1	81	1 1 88 88 27
min distant	Jeunyi cave was more things	Product	C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH(C <sub>3</sub> H <sub>7</sub> -i)C(C <sub>3</sub> H <sub>7</sub> -n)CO <sub>2</sub> C <sub>2</sub> H <sub>6</sub> ) <sub>2</sub> Diethyl n-propyl-(\$-cyclopentylethyl)- malonate	Diethyl n-propyl-(\$-eyclohexylethyl)-	malonato $C_{\mathfrak{d}}\Pi_{\mathfrak{z}}O(C\Pi_{\mathfrak{z}})_{\mathfrak{z}}C(C_{\mathfrak{z}}\Pi_{\mathfrak{z}}\cdot n)(CO_{\mathfrak{z}}C_{\mathfrak{z}}\Pi_{\mathfrak{z}})_{\mathfrak{z}}$	Dietliyl 11-propyl-(y-cyclohexylpropyl)-	malonato $C_6 II_5 O(CII_2)_3 C(C_3 II_7 \cdot n)(CO_2 C_2 II_5)_2$	$n$ - $C_{10}H_{21}\mathrm{C}(C_{2}H_{7}\text{-}n)(\mathrm{CO}_{2}C_{2}H_{2})_{2}$ Dicthyl $n$ -propyl-(4-eyelohexylbutyl)- malozate	n-C <sub>11</sub> H <sub>23</sub> C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>12</sub> H <sub>23</sub> C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> Dicklyi n-propyl-[β-(Γ-naphliyt)ethyl]-	niconne niconne n-C <sub>13</sub> H <sub>27</sub> (C <sub>2</sub> H <sub>2</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> ) <sub>2</sub> n-C <sub>14</sub> H <sub>22</sub> (C <sub>2</sub> H <sub>2</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> ) <sub>2</sub> n-C <sub>14</sub> H <sub>22</sub> (C <sub>3</sub> H <sub>2</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> ) <sub>2</sub> Dicthyl cyclobutane 1, 1-dicarboxylate Dicthyl cyclobutane 1, 1-dicarboxylate
Holf off	(THE CA	Agent	C <sub>7</sub> i-C <sub>2</sub> U <sub>7</sub> CHBrCO <sub>2</sub> C <sub>2</sub> U <sub>5</sub> β-Cyclopentylcthyl bromide	$C_8$ eta-Cyclohexyletliyl bromide	CollsO(CH2)2th	$C_{g}$ $\gamma$ -Cyclohexylpropyl bromide	C <sub>3</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>3</sub> Cl	$G_{10}$ $n\text{-}G_{10}H_{21}X_{+}^{*}$ $\delta\text{-}Cyclohexylbutyl bromide}$	C <sub>11</sub> -C <sub>16</sub> n-C <sub>11</sub> H <sub>23</sub> X. n-C <sub>12</sub> H <sub>25</sub> X.† \(\rho_{-}(1-Naplithy!)etliy!\) bromide	n-C <sub>13</sub> H <sub>27</sub> X; n-C <sub>14</sub> H <sub>29</sub> X; n-C <sub>16</sub> H <sub>23</sub> I
			Cont.)							

545 172 277 282	125 531 120 015 556	44, 51 203 125 553 126 334 501 11	125 653 017 017 203 126 553 126 553 120 912
Ethanol Ethanol Ether-ethanol Ethanol	Toluene Ethanol Toluene Ethanol	(C <sub>2</sub> II <sub>5</sub> O) <sub>2</sub> CO C <sub>6</sub> II <sub>5</sub> -ether Tolueno Toluene Toluene Ethunol	Toluene Toluene Ethanol Toluene C <sub>d</sub> H <sub>d</sub> -ether Toluene Toluene Ethanol Ethanol
$NaOC_2H_5$ $NaOC_2H_5$ $NaNI_2$ $NnOC_2II_5$	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>6</sub> NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	NAOC <sub>2</sub> H <sub>3</sub> NANH <sub>2</sub> NAOC <sub>3</sub> H <sub>3</sub> NAOC <sub>2</sub> H <sub>3</sub> NAOC <sub>2</sub> H <sub>5</sub> NAOC <sub>2</sub> H <sub>5</sub>	NaOC2H3 NaOC2H3 NaOC2H3 NaOC2H3 NaNU12 NaOC2H3 NaOC2H3 NaOC2H3 NaOC2H3 NaOC2H3 NaOC2H3
70-85 — 26 ca. 70	40 70-00 —	83 83 70-90 70-90 86 1	70-90 70-75 82 70-90 70-90 70-90 Poor 20 68
$C_2H_5C(C_3H_5)(CO_2C_2H_5)_2$ $B_1C(G_2)_2C(C_3H_3)(CO_2C_2H_5)_2$ $B_1CH = CHC(C_3H_5)(CO_2C_2H_5)_2$ $C(H_2)_2CH(C_3H_5)$ $C_2C_3C_3C_3C_3C_3C_3C_3C_3C_3C_3C_3C_3C_3C$	C <sub>2</sub> H <sub>5</sub> SCH <sub>2</sub> C(C <sub>3</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> ··C <sub>3</sub> H <sub>5</sub> C(C <sub>3</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> CH <sub>3</sub> SCH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> (C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> C(CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> (CH <sub>3</sub> ) <sub>2</sub> C(NO <sub>2</sub> )C(C <sub>3</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	n-c <sub>1</sub> H <sub>2</sub> C(C <sub>2</sub> H <sub>2</sub> )(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sup>2</sup> C <sub>2</sub> H <sub>3</sub> OCH(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>3</sub> )(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sup>2</sup> n-C <sub>3</sub> H <sub>3</sub> S(CH <sub>2</sub> )C(C <sub>3</sub> H <sub>3</sub> )(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sup>2</sup> C <sub>3</sub> H <sub>3</sub> S(CH <sub>2</sub> ) <sup>2</sup> C(C <sub>3</sub> H <sub>3</sub> )(Co <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sup>2</sup> C <sub>3</sub> H <sub>3</sub> S(CH <sub>3</sub> ) <sup>2</sup> C(C <sub>3</sub> H <sub>3</sub> )(Co <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sup>2</sup> Diethyl allyl(cyelobutylmethyl)malonato CH <sub>3</sub> CCl=CHCH <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> )(Co <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) CH <sub>2</sub> =CHCHCH <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> )(Co <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) CH <sub>2</sub> =CHCHCH <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> )Co <sub>3</sub> C <sub>2</sub> H <sub>3</sub>	$n$ -C, $\mu_3$ CCH <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ), $n$ -C <sub>3</sub> H <sub>3</sub> S(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>2</sub> H <sub>3</sub> ), $n$ -C <sub>3</sub> H <sub>3</sub> C(CH <sub>3</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ), $n$ -C <sub>3</sub> H <sub>3</sub> C(H(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>3</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>3</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>3</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> )(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ), $n$ -C <sub>4</sub> H <sub>3</sub> CCH <sub>4</sub> CH <sub>3</sub> C <sub>4</sub> H <sub>3</sub> CC  <sub>4</sub> CH <sub>3</sub> CC <sub>4</sub> H <sub>3</sub> CCC <sub>4</sub> CC <sub>4</sub> H <sub>3</sub> CCC <sub>4</sub> CC <sub>4</sub> H <sub>3</sub> CCC <sub>4</sub> CC <sub>4</sub> H <sub>3</sub> CCCC <sub>4</sub> CC <sub>4</sub> H <sub>3</sub> CCCC <sub>4</sub> CC <sub>4</sub> H <sub>3</sub> CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
$C_3$ $C_2H_5Br$ $Br(CH_2)_2Br$ $BrCH = CHBr$ $CH_2 \longrightarrow CH_2$ $C_3$	$C_2\Pi_4$ SOH <sub>2</sub> CI $i$ - $C_3\Pi_4$ Br $CH_3$ SCH(CH <sub>3</sub> )CI $CH_2$ == $CHCH_3$ Br $CH_2$ = $CHCH_2$ Br $C_4$	$n$ - $C_4H_9$ Br $C_2H_5$ OCH(CH <sub>3</sub> )Cl $n$ - $C_4H_5$ SCH <sub>4</sub> Cl $C_2H_5$ SCH( $G_1$ )Cl $C_2H_5$ SCH( $G_1$ )Cl $C_2H_3$ SCH( $G_1$ )Cl $C_2H_3$ SCH( $G_1$ )Cl $C_1$ Cl $C$ Cl $C$ Cl $C$ Cl CCl $C$ Cl $C$ Cl $C$ Cl $C$ Cl CCl $C$ Cl $C$	$\begin{array}{c} n \cdot c_3 H_3 S C H_2 C I \\ n \cdot c_3 H_3 S C H_2 I_2 C I \\ n \cdot c_3 H_4 S C H_2 C I C I I_3 I_2 C I \\ n \cdot c_3 H_4 C I C C I I_3 I_3 C I C I C I_3 I_3 C I C I C I_3 I_3 C I C I C I_3 I_4 C I C I C I_3 I_5 C I C I I_5 C I I_5 C I I_5 C I I_5 C I C I I_5 C I C I I_5 C I C I C I I_5 C I C I I_5 C I C I C I I_5 C I I_5 C I C I I_5 C I I I I C$
$CH_2 = CMCH_2$ $(= C_3H_3)$			

Note: References 577-1080 are ‡ The halogen was not specified.

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TABLE III-Continued

ALKYLATION OF MONOALKYLMALONIC ESTERS, R'CII(CO2R)?

Hanel . Tolucar Ethanal Solvent Sa0C<sub>3</sub>H<sub>3</sub> NaOC. III3 NaOC<sub>2</sub>11<sub>5</sub> Base (The diethyl ester was used unless otherwise indicated.) Yield.  $\frac{n\cdot C_3\Pi_{11}C(C_3\Pi_{7^{-1}})(CO_3C_3\Pi_3)_3}{n\cdot C_4\Pi_3^{-1}SC\Pi_3^{-1}C(C_3\Pi_{7^{-1}})(CO_2C_3\Pi_3)_3}$ Product Alkylating n-C,111,SCHI,CI Agent n-C<sub>3</sub>H<sub>11</sub>Br

ence

222

필무취원받

(C,11,0),CO

(thanel

NaOC; II; NaOC; II;

Cansolcencenalereausoccosesins)  $(CH_2)_2 C = CHCH_2 C(C_3H_7)(CO_3C_3H_2)_3$  $(c_1)_1 C = C \prod_1 C (c_2) \prod_2 C (C c_2)_1$ 

Cansoaccus, cican, 1000 Calls

Mone

tour:

NaOC.115

Poor 100 73

c. . . 0

i.C,II,C(C,II,-1)(CO,C,II,)3

(CII3)3C=CIICII3Br (CII3),C=CIICII,Br CIT,CIIInCO,C,IIS (Cir,),CO,C,IIs

i.C, II, Br

i-C, II, (Cont.)

'n

NaO('115

None	Teluros Toluros Ritaros Ribaros	Ethaned (C <sub>2</sub> II <sub>3</sub> O) <sub>3</sub> CO
Ā	# # # #	มี <b>ย</b>
ž.	NaOC; II; NaOC; II; NaOC; II; NaOC; II;	NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub>
1	70-80 70-90 Pear Pear	15
Diethyl (sopropyl-(2-thenyl)malomate	n-C,III,\$(CII),}(Y(C <sub>3</sub> II)-1XCO <sub>3</sub> C <sub>3</sub> III,) <sub>1</sub> n-C,III,\$CII(CII,\$CC <sub>3</sub> II)-1XCO <sub>3</sub> C <sub>3</sub> III,) <sub>2</sub> C,III,O,CCII(CI <sub>3</sub> II,XYCC <sub>3</sub> II <sub>3</sub> -1XCO <sub>3</sub> C <sub>3</sub> III,) <sub>3</sub> C <sub>3</sub> II <sub>3</sub> O <sub>4</sub> (CYCII(CI) <sub>3</sub> I <sub>2</sub> C(C <sub>3</sub> II <sub>3</sub> -1XCO <sub>3</sub> C <sub>3</sub> II <sub>3</sub> ) <sub>3</sub>	None CettsCttsC(Cetts-i)(COsCetts)s
I(CII <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> 2-Chloromethylthlophene	O4 n-C,H,S(CH,),Cl n-C,H,SCH(CH,)Cl C,H,CHRrCO4C,H, (CH,),CBrCO4C,H,	<i>C,</i> i-c,ii,ciiisco,c,ii, C,ii,cii,ci C,-C,

3 \$ 3 ¥ 45

Nylene

ž

5

Diethyl kopropyl-(2,5-dimethylbenzyl)-

n-C<sub>13</sub>II<sub>27</sub>C(C<sub>2</sub>II<sub>7</sub>-0)(CO<sub>2</sub>C<sub>2</sub>II<sub>2</sub>)<sub>2</sub>

majorate

2,5.Dimethylbenzyl chloride

n-C13H37X\$

Centocular

nc \_\_\_\_ c(c,11,000,c,11,

Ethand

NaOC, II,

l

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Ethanol

NaOC, II,

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## TABLE III-Continued

Alkylation of Monoalkylmalonic Esters,  $\mathrm{R'CH}(\mathrm{CO}_2\mathrm{R})_2$ (The diethyl ester was used unless otherwise indicated.)

Refer-	ence	553 126 126 808 530 223	554 223 506	914 902 510 11	920	920 902 509 920
	Solvent	Toluene Toluene Toluene Ethanol Ethanol	Toluene Ethanol	Xylene Ethanol Ethanol Ethanol	Bthanol Bthanol	Ethanol Ethanol Toluene Ethanol
	Base	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	$Na$ $NaOC_2H_6$ $NaOC_2H_5$ $NaOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>6</sub>
V. Joly	, we will also with a second s	70-90 70-90 70-90 10-90	5 - 55	1128	17	%
(TITE CITED TO THE CITED OF THE	Product	$\begin{array}{ll} & \text{r-c}_1 \Pi_3 \text{S(CII)}_2 \text{S(C}_3 \Pi_3) \text{CO}_2 \text{C}_2 \Pi_3)_2 \\ & \text{r-c}_1 \Pi_3 \text{CCH(CII}_3) \text{CO}_2 \text{C}_3 \Pi_3)_2 \\ & \text{r-c}_1 \Pi_3 \text{CCH(CII}_3) \text{CC}_3 \Pi_3)_2 \\ & \text{CH}_2 = \text{CCH}_3 \text{CCH(C}_3 \Pi_3) \text{CC}_3 \text{C}_3 \Pi_3)_2 \\ & \text{C}_3 \Pi_5 \text{O}_2 \text{CCH}_3)^2 \text{CC}_3 \Pi_3 \text{CC}_3 \Pi_3)^2 \text{CC}_3 \Pi_3 \text{CC}_3 \Pi_3)_2 \\ & \text{c}_3 \Pi_5 \text{O}_2 \text{CC(CII}_3)^2 \text{CC}_3 \Pi_5) \text{CO}_2 \text{C}_2 \Pi_3)_2 \end{array}$	n-C <sub>1</sub> H <sub>5</sub> SCH <sub>2</sub> CH(CH <sub>5</sub> )C(C <sub>3</sub> H <sub>5</sub> )CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>3</sub> H <sub>3</sub> O <sub>3</sub> CCH(C <sub>3</sub> H <sub>5</sub> +i)C(C <sub>3</sub> H <sub>3</sub> )CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C(C <sub>3</sub> H <sub>6</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	n-C <sub>4</sub> H <sub>2</sub> CH(C <sub>2</sub> H <sub>3</sub> )CH <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Dichlyl allyl-(G-cyclohoxylchyl)malonate H <sub>3</sub> C <sub>6</sub> CHCH <sub>2</sub> C(C <sub>3</sub> H <sub>3</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> O——CO	$\textit{n-C}_{\mathfrak{g}}H_{19}C(C_3H_{\mathfrak{g}})(CO_3C_2H_{\mathfrak{g}})_2$ Diethyl allyl-(\$\psi\$-cyclohexylpropyl)malonate	$\begin{array}{l} n\text{-}C_{10}\text{H}_{21}\text{C}(C_{3}\text{H}_{3})\text{C}O_{2}C_{2}\text{H}_{5})_{2} \\ \text{Diethyl allyl-}(\delta\text{-}cyclohexylbutyl)\text{malonate} \\ p\text{-}i\text{-}C_{3}\text{H}_{1}\text{C}\text{H}_{4}\text{C}\text{H}_{5}\text{C}(C_{3}\text{H}_{3})\text{C}O_{2}C_{2}\text{H}_{5})_{2} \\ n\text{-}C_{11}\text{H}_{22}\text{C}(C_{3}\text{H}_{3})\text{C}O_{2}^{C}C_{2}\text{H}_{5})_{2} \end{array}$
n all T	Alkylating Agent	C <sub>6</sub> n-C <sub>4</sub> H <sub>5</sub> S(CH <sub>2</sub> ) <sub>2</sub> Cl n-C <sub>4</sub> H <sub>5</sub> SCH(CH <sub>3</sub> )Cl cH <sub>2</sub> -m <sub>2</sub> CCH(CH <sub>3</sub> )Cl CH <sub>2</sub> -m <sub>2</sub> CCH <sub>3</sub> CH(C <sub>2</sub> H <sub>5</sub> )Cl Br(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> (CH <sub>3</sub> ) <sub>2</sub> ChrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	C, n-C,II,\$CH <sub>2</sub> CH <sub>2</sub> CH(CH <sub>3</sub> )Cl i-C <sub>3</sub> II,CHBrCO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> C <sub>3</sub> II <sub>3</sub> CH <sub>2</sub> Cl	C <sub>8</sub> n-C <sub>1</sub> II <sub>2</sub> CII(C <sub>2</sub> II <sub>3</sub> )CII <sub>2</sub> Br β-Cyclohexylethyl bromide o-Methylbenxyl bromide H <sub>2</sub> C <sub>6</sub> CII—CII <sub>2</sub>	$c_{ m 9}$ $n$ - $c_{ m 9}H_{ m 19}{ m Br}$ $\gamma$ -Cyclohexylpropyl bromldc	C <sub>10</sub> -C <sub>12</sub> n·C <sub>10</sub> H <sub>21</sub> Br ∂-Cyclohexylbutyl bromlde p·i·C <sub>2</sub> H <sub>4</sub> Ch <sub>4</sub> CH <sub>2</sub> Cl n·C <sub>11</sub> H <sub>23</sub> Br
	π,	CH3 CUCH2 (Cont.)				

TABLE III-Continued

ALKYLATION OF MONOALKYLMALONIC ESTEUS R'CH(CO2R), (The dethyl ester was used unless otherwise indicated.)

R. n.C.H. (Cod.)

Refer-	ence	125, 803 915 1.48 656, 129 656	141 141 44 203 541 126 277	916, 917	125 545 545 545 44 553
	Solvent	Tolnene Ethanol Ethanol None Ether	Ethanof Ethanof (C <sub>2</sub> 11 <sub>2</sub> 0) <sub>2</sub> CO C <sub>6</sub> H <sub>6</sub> -ether Ethanol Toluene Ether	Ethanol Ethanol	Toluene Ethanol (C <sub>4</sub> H <sub>5</sub> O) <sub>2</sub> CO Toluene
	Ваяе	NaOC, II; NaOC, II; NaOC, II; Na	NaOC <sub>2</sub> II <sub>3</sub> NaOC <sub>2</sub> II <sub>3</sub> NaOC <sub>2</sub> II <sub>4</sub> NaOC <sub>2</sub> II <sub>4</sub> NaOC <sub>2</sub> II <sub>4</sub> NaOC <sub>2</sub> II <sub>5</sub> Na	NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub>	NaOC <sub>2</sub> H <sub>3</sub>
. :	Ylekt.	75 80 80 80 80	74 70 68 70-50 70-90 68 56	30	70-85 70-85 78 70-90
(The diethyl ester was used inness com.	Product	C3.II,SCII,4C(C4.II,***)CO3.C4.II,3); C1I,***:C1CII,4C(C4.II,***)CO3.C4,II,3); INCII,3,C(C4.II,***)CO3.C4,II,3); INCII,3,C(C4.II,***)CO3.C4,II,3);	$(m.c_1\mu_3, C(CO_1C_1\mu_3), \\ (m.c_1\mu_3, C(CO_1C_1\mu_3), \\ (m.c_1\mu_3, C(C_1\mu_3), C(C_1\mu_3), \\ (c_1\mu_3, C(C_1\mu_3), C(C_1\mu_3), C(C_2\mu_3), \\ (c_1\mu_3, C(C_1\mu_3), C(C_2\mu_3), \\ (c_1\mu_3, C(C_1\mu_3), C(C_2\mu_3), \\ (c_1\mu_3, C(C_2\mu_3), C(C_2\mu_3), \\ (c_1\mu_3, C(C_2\mu_3$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	n-C <sub>4</sub> II,SCII,C(C <sub>4</sub> II,n)(CO <sub>4</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>4</sub> II,C(II,)Q(C <sub>4</sub> II,n)(CO <sub>4</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>4</sub> II,C(II(C <sub>4</sub> II),Q(C <sub>4</sub> II,n)(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> i-C <sub>4</sub> II,Q(C <sub>4</sub> II,n)(CO <sub>4</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>4</sub> CII <sub>2</sub> =CIIC(II,SCIC(I) <sub>4</sub> I <sub>3</sub> ) <sub>4</sub> CII <sub>2</sub> =CIIC(II,SCII) <sub>4</sub> (CII <sub>4</sub> I <sub>4</sub> -n)(CO <sub>4</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>4</sub> Dictiy1 cyclopentyI-(n-butyl)nnlonate
ALL)	Alkyladna Agraf	C <sub>3</sub> C <sub>4</sub> H <sub>2</sub> SCH <sub>4</sub> Cl cC <sub>4</sub> H <sub>2</sub> H <sub>2</sub> CH <sub>4</sub> -CHCH <sub>4</sub> H <sub>2</sub> Hr(CH <sub>2</sub> )H <sub>2</sub> (CH <sub>3</sub> ) <sub>2</sub> CCH <sub>3</sub> O <sub>3</sub>	Cincelline  n-Cilline  recilline  cillinetten  cillinette	CH,CCT = CHCH,CL CH, CHCH CH,	C <sub>3</sub> n-c <sub>1</sub> u <sub>3</sub> ccu <sub>4</sub> ctl  c <sub>1</sub> u <sub>3</sub> cu(cu <sub>1</sub> u)nr  c <sub>1</sub> u <sub>3</sub> cu(cu <sub>1</sub> u)nr  i-c <sub>1</sub> u <sub>3</sub> u <sub>1</sub> nr  i-c <sub>1</sub> u <sub>1</sub> nr  c <sub>1</sub> u <sub>1</sub> u <sub>1</sub> nr  c <sub>2</sub> u <sub>1</sub> u <sub>1</sub> nr  c <sub>2</sub> u <sub>1</sub> u <sub>1</sub> nr

	THE	ALKY	CLATIC	ON OF	ESTE	RS AND	NITRILES	
897 918	641, 919 641 399 725	121, 142, 143 900	545 902	142	887 902	142 888 902	887 920 906, 883 135 684	532 657
None Ethanol	Ethano Ethanol Ethanol	Ethanol Ethanol	Ethanol Ethanol	Ethanol Ethanol	Ethanol Ethanol	Ethanol Ethanol Ethanol	Ethanol Ethanol Toluene Ethanol n-C <sub>4</sub> H <sub>9</sub> OH	None Ethanol
$_{ m Na}$	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	$NaOC_2H_5$ $NaOC_2H_5$	$NaOC_2H_5$ $NaOC_2H_5$	$ m NaOC_2H_6 \ NnOC_2H_5$	NaOC2H5 NaOC2H5	NaOC2H s NaOC2H s NaOC2H s	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> Na NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>4</sub> H <sub>9</sub> -n	Na NaOC <sub>2</sub> H <sub>5</sub>
ដ	1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	70	70-85	44 50	1.1	នារ	1   528 00	17
Diethyl n-butyl-(2-thenyl)malonate n-G <sub>4</sub> H <sub>0</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> )2C(CH <sub>3</sub> )2- CH <sub>2</sub> C(C <sub>4</sub> H <sub>3</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> )2	n-C <sub>6</sub> H <sub>13</sub> C(C <sub>4</sub> H <sub>9</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>7</sub> H <sub>13</sub> C(C <sub>4</sub> H <sub>9</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>7</sub> H <sub>15</sub> C(C <sub>4</sub> H <sub>9</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyl n-butyl-(f-cyclopentylethyl)-	$ \min_{\mathbf{G} \in \mathcal{M}_{\mathbf{G}}} \min_{\mathbf{G} \in \mathcal{G}_{\mathbf{G}}} \max_{\mathbf{G} \in \mathcal{G}_{\mathbf{G}}} (\mathbf{G}_{\mathbf{G}}^{H}, \mathbf{g}, n) (\mathbf{GO}_{\mathbf{G}}^{C} \mathbf{G}_{\mathbf{G}}^{H}, \mathbf{g})_{\mathbf{Z}} \\ p_{-1} \mathbf{G}_{\mathbf{G}}^{H} \mathbf{H}_{\mathbf{G}}^{H} \mathbf{H}_{\mathbf{G}}^{H} \mathbf{G}(\mathbf{G}_{\mathbf{G}}^{H}, \mathbf{g}-n) (\mathbf{GO}_{\mathbf{G}}^{C} \mathbf{G}_{\mathbf{G}}^{H}, \mathbf{g})_{\mathbf{Z}} $	$n \cdot C_6 \Pi_{19} CH(C\Pi_9) C(C_4 \Pi_9 \cdot n) (CO_2 C_2 \Pi_5)_2$ Diethyl $n \cdot \text{butyl} \cdot (\beta \cdot \text{eydlobexylethyl})_2$		$\dot{O} = \dot{C}O$ $n \cdot C_0 \Pi_{19} C(C_4 \Pi_9 \cdot n)(CO_2 C_2 \Pi_5)_2$ Dielity! $n \cdot b \cdot u t y! \cdot (y \cdot e y c lo h e x y) propy!)$	into min $C_1 = C_2 + C_2 + C_3 + C$	n-C <sub>11</sub> H <sub>23</sub> C(C <sub>4</sub> H <sub>9</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyl undecenyl-(n-butyl)malonate n-C <sub>12</sub> H <sub>35</sub> C(C <sub>4</sub> H <sub>9</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>16</sub> H <sub>35</sub> C(C <sub>4</sub> H <sub>9</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>20</sub> H <sub>44</sub> C(C <sub>4</sub> H <sub>9</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	i-C <sub>4</sub> H <sub>9</sub> C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> i-C <sub>4</sub> H <sub>9</sub> C(C <sub>2</sub> H <sub>5</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>
$2 ext{-Chloromethylthiophene}$ (CH $_3$ ) $_2$ C(CH $_2$ Br) $_2$	C <sub>6</sub> −C <sub>7</sub> n-C <sub>6</sub> H <sub>13</sub> Br n-C <sub>7</sub> H <sub>15</sub> Br n-C <sub>7</sub> H <sub>15</sub> I β-Cyclopentylethyl bromide	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cl p-IC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	$C_8$ – $C_{10}$ $n$ - $C_6$ H $_{13}$ CH(CH $_3$ )Br eta-Cyclohexylethyl bromlde	$C_6H_5(CH_2)_2Br$ $H_5C_6CH_2$	$^{\circ}$ O' $^{\circ}$ $^{\circ}$ C $_{9}\Pi_{19}X^{+}_{2}$ $^{\circ}$ Cyclohexylpropyl bromide	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>3</sub> X; n-C <sub>10</sub> H <sub>21</sub> X; 5-Cyclohexylbutyl bromide	C <sub>11</sub> -C <sub>20</sub> n-C <sub>11</sub> H <sub>22</sub> -X; Undecenyl bromide n-C <sub>12</sub> H <sub>23</sub> .I n-C <sub>12</sub> H <sub>23</sub> I n-C <sub>16</sub> H <sub>33</sub> I C <sub>5</sub> -C <sub>20</sub> H <sub>41</sub> I C <sub>5</sub> -C <sub>5</sub>	C <sub>2</sub> H <sub>5</sub> Br C <sub>2</sub> H <sub>5</sub> I

 $\begin{array}{c} C_2H_5\mathrm{Br}\\ C_2H_5\mathrm{I}\\ \end{array}$  Note: References 577–1080 are on pp. 322–331.  $\ddag$  The halogen was not specified.

## TABLE III—Continued

Alkylation of Monoalkylmalonic Esters,  $R'CH(CO_2R)_2$  (The diethyl ester was used unless otherwise indicated.)

R' i-C<sub>4</sub>H<sub>9</sub> (Cont.)

Refer-	ence 125 555	172	125 556	642 44 126	125, 893 657 126, 899	223 708	223 223	223 888
	Solvent Toluene C <sub>6</sub> II <sub>6</sub>	Ethanol	Toluene Bither	Ethanol $(C_2 II_5 O)_2 CO$ Toluene	Toluene Ethanol Toluene	Ethanol None	Ethanol Ethanol	Ethanol Ethanol
	Base NaOC <sub>2</sub> H <sub>5</sub> Na	$NaOC_2H_5$	NaOC <sub>2</sub> II <sub>s</sub> Na	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	$ m NaOC_2H_5$ m Nn	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	$\rm NaOC_2H_5$ $\rm NaOC_2H_5$
Page A	% % % % % % % % % % % % % % % % % % %	ļ	1 8	76 76 70-90	73 70-90	12	10 13	Poor
(The diethyl ester was used unless outer with	$\begin{array}{c} \text{Product} \\ \text{CH}_3\text{SCH}_2\text{C}(C_4\text{II}_5^{-4})\text{CO}_2\text{C}_2\text{II}_5)_2 \\ \text{(CH}_2)_2^{-1}\text{C}(C_4\text{III}_5^{-4})\text{CO}_2\text{C}_2\text{II}_5 \end{array}$	CO  CO Br(CH <sub>2</sub> )2C(C <sub>4</sub> H <sub>9</sub> -i)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> )2	$C_2H_5\mathrm{SCH}_2\mathrm{C}(C_4\Pi_9\cdot\mathrm{i})\mathrm{CO}_2C_3\Pi_6)_2$ (CH $_3$ ) $_2\mathrm{C}(\mathrm{NO}_2)\mathrm{C}(C_4\Pi_9\cdot\mathrm{i})\mathrm{CO}_2\mathrm{C}_2\Pi_5)_2$	(i-C <sub>4</sub> II <sub>4</sub> ) <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> (i-C <sub>4</sub> II <sub>5</sub> ) <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> II <sub>5</sub> SCII(CII <sub>3</sub> )C(C <sub>4</sub> II <sub>5</sub> -i)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub>	n-C <sub>4</sub> H <sub>5</sub> SCH <sub>5</sub> C(C <sub>4</sub> H <sub>5</sub> -i)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> i-C <sub>5</sub> H <sub>1</sub> C(C,H <sub>5</sub> -i)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CH <sub>c=</sub> CHCH <sub>5</sub> SCH(CH <sub>3</sub> )-	C(C <sub>4</sub> H <sub>9</sub> -i)(ĈO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>z</sub> C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH(CH <sub>3</sub> )C(C <sub>4</sub> H <sub>3</sub> -i)(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> Dictityl z-butyl-(2-thenyl)malonate	$\begin{array}{l} C_{2}\Pi_{5}O_{2}CCH(C_{2}\Pi_{3})C(C_{4}\Pi_{5}^{-4})(CO_{2}C_{2}\Pi_{5})_{2} \\ C_{2}\Pi_{5}O_{2}CC(C\Pi_{5})_{2}C(C_{4}\Pi_{5}^{-4})(CO_{2}C_{2}\Pi_{5})_{2} \end{array}$	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH(C <sub>5</sub> H <sub>7</sub> -3)C(C <sub>4</sub> H <sub>5</sub> -3)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>10</sub> H <sub>21</sub> C(C <sub>4</sub> H <sub>5</sub> -3)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>
(The d	Alkylating Agent CH <sub>3</sub> SCH <sub>2</sub> Cl DrCH <sub>2</sub> CH <sub>2</sub> Br	$\mathrm{Br}(\mathrm{CH}_2)_2\mathrm{Br}$	G, C,H,SCH,Cl (CH,3),CClNO,	O4 i-C,U,Br i-C,U,Br C <sub>2</sub> U,SCH(CH <sub>2</sub> )Cl	C <sub>5</sub> n-C <sub>4</sub> H <sub>9</sub> SCH <sub>2</sub> Cl i-C <sub>4</sub> H <sub>1</sub> Bi n-C <sub>4</sub> H <sub>2</sub> SCH <sub>2</sub> Cl	$CH_3 = CHC_1 SCHOLT_2 SCHOLT_3 SCHOLT$	$C_6$ $C_2$ $U_5$ $CHB_1$ $CO_2$ $C_2$ $H_5$ $(CH_3)_2$ $CB_1$ $CO_2$ $C_2$ $H_5$	$c_7$ - $c_{12}$ $i$ - $c_3$ H,cIIBrCO $_2$ C $_2$ H $_5$ $n$ - $c_{10}$ H $_2$ IX $^+$

=							
888 482, 481	148	227 146 330 125	125 44, 51 203	330	125 147 144 561	561 125 125	552 552
Ethanol Ethanol	Ethanol $(C_2\Pi_5O)_2CO$	Ethanol (C <sub>2</sub> 11 <sub>5</sub> 0) <sub>2</sub> CO Toluene	Toluene (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO C <sub>6</sub> H <sub>6</sub> -ether	$(C_211_5O)_2CO$ $(sec-C_4H_9O)_2CO$ $(sec-C_411_9O)_2CO$	(C <sub>2</sub> H <sub>3</sub> O) <sub>2</sub> CO Toluene (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO	Toluene Toluene	Ethanol
$ m NaOC_2H_5 \ NaOC_2H_5$	$NaOC_2H_5$ $NaOC_2H_5$	$NaOC_2H_5$ $NaOC_2H_5$ $NaOC_2H_5$	$ m NaOC_2H_5 \ NaOC_2H_5 \ NaNH_2$	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>4</sub> H <sub>9</sub> -sec NaOC <sub>4</sub> H <sub>9</sub> -sec	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> 		NaOC <sub>2</sub> II <sub>5</sub>
1 %	Poor 95	Poor Poor	88 84	15 25 (59)§ Poor	84 	81111	I
n-C <sub>1,2</sub> II <sub>3,2</sub> CC <sub>4</sub> II <sub>3</sub> -iXCO <sub>2</sub> C <sub>2</sub> H <sub>3,2</sub> Dietliyl 3-methyleyclobutane-1,1- diearboxylate	$C_2H_5C(C_4H_6\text{-see})(GO_2C_2\Pi_5)_2$ $C_2\Pi_5C(C_4H_6\text{-see})(GO_2C_2\Pi_5)_2$	C <sub>2</sub> H <sub>2</sub> C(C <sub>4</sub> H <sub>3</sub> -sre)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>3</sub> C(C <sub>4</sub> H <sub>3</sub> -sre)(CO <sub>3</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> CH <sub>3</sub> SCH <sub>2</sub> C(C <sub>4</sub> H <sub>3</sub> -sre)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	$\begin{array}{l} C_2H_3SOH_2C(C_4H_9\text{-}seo)(CO_2C_2H_3)_2\\ C\Pi_2=CHG\Pi_2C(C_4H_9\text{-}seo)(CO_2C_2H_3)_2\\ C_2H_3OCH(C\Pi_3)C(C_4\Pi_3\text{-}seo)(CO_2C_2H_3)_2 \end{array}$	(sec-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (sec-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> C(CO <sub>2</sub> C <sub>4</sub> H <sub>9</sub> -sec) <sub>2</sub> §§ (sec-C <sub>4</sub> H <sub>9</sub> ) <sub>2</sub> C(CO <sub>2</sub> C <sub>4</sub> H <sub>9</sub> -sec) <sub>2</sub> §§	$\begin{array}{ll} n \cdot G_2 H_1 C (C_4 H_2 \cdot sec) (CO_2 C_2 H_2)_2 \\ n \cdot C_4 H_3 S C H_2 C (C_4 H_2 \cdot sec) (CO_2 C_2 H_3)_2 \\ v \cdot C_3 H_1 C (C_4 H_4 \cdot sec) (CO_2 C_2 H_3)_2 \\ C H_2 = C H C H_2 C (C_4 H_3 \cdot h) (CO_2 C_2 H_3)_2 \\ C H_3 C C I = C H C H_2 (C_4 H_3) (CO_2 C_4 H_3)_2 \\ (C H_3 C C I = C H C H_4 C (C_2 H_3) (C C_3 H_3)_2 \\ (C H_3 C C I = C H C H_3)_2 C (CO_3 C_4 H_3)_2 \end{array}$	$CH_3CCI = CHCH_2(Ct_{H1-7})(Ct_2C_2H_3);$ $CH_2 = C(CH_3)CH_2(Ct_{H1-7})(Ct_2C_3H_3);$ $CH_2 = C(CH_3)CH_2(C(CH_3)CH_3)(Ct_2H_3);$ $CH_2 = C(CH_3)CH_2(C(CH_3)C_3H_3);$ $CH_3 = C(CH_3)CH_2(Ct_3H_7-7)(Ct_2H_3);$ $CH_4 = C(CH_3)CH_2(Ct_3H_7-7)(Ct_2H_3);$	C112 = ((CH3)CH2C(C3H7-i)(CO2C2H5)2
n-C <sub>12</sub> H <sub>25</sub> X‡ None C <sub>2</sub>	C <sub>2</sub> H <sub>5</sub> Br C <sub>2</sub> H <sub>5</sub> Br	$C_2H_3^1$ $(C_2H_3O)_2CO$ $CH_3SOH_2CI$ $C_3$	$C_2H_3SCH_2CI$ $CH_2 = CHCH_2Dr$ $C_2H_3OCH(CH_3)CI$ $C_4$	sec-C <sub>4</sub> H <sub>5</sub> Br sec-C <sub>4</sub> H <sub>5</sub> Br (sec-C <sub>4</sub> H <sub>5</sub> O) <sub>2</sub> CO C <sub>5</sub>	n-C <sub>6</sub> H <sub>11</sub> Br n-C <sub>4</sub> H <sub>2</sub> SCH <sub>2</sub> Cl +C <sub>2</sub> H <sub>11</sub> Br CH <sub>2</sub> = CHCH <sub>2</sub> Dr C <sub>2</sub> H <sub>2</sub> X‡ CH <sub>3</sub> CO =CHCH <sub>2</sub> Cl	i-c, H <sub>1</sub> X* CH <sub>3</sub> SCH <sub>3</sub> Cl C <sub>4</sub> H <sub>5</sub> SCH <sub>2</sub> Cl n-c, H <sub>5</sub> X* i-c, H <sub>5</sub> X*	Note: References 577-1080 are on pp. 322-331. The halogen was not specified. How and to any
Clch2ckch3)ch2	sec-C <sub>4</sub> H <sub>9</sub>				ŀC,H9 CH3CCl=CHCH2	$\mathrm{CH}_2\!=\!\mathrm{C}(\mathrm{CH}_3)\mathrm{CH}_2$	Nate: References 577-1050 are # The halogen was not specified.

I Here and in subsequent cases the first figure represents the conversion; the figure in parentheses represents the yield.

TAILE III Continued

us, R'CH(CO <sub>2</sub> R) <sub>2</sub>	gae indiented.)
ALEVIATION OF MONOALEVEMALONIC ESTIMS, R'UH(CO2B);	(The dealigt exter was used unless otherwise indicated.)
71.5	`_

						7,000
	Alle fatted.	4.001	Yield,	Have	Solvent	ence.
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	equiv.competix:	CH <sub>1</sub> - C(CH <sub>2</sub> )CH <sub>2</sub> CC <sub>1</sub> H <sub>2</sub> · oc)CO <sub>2</sub> C <sub>1</sub> H <sub>3</sub> · CH <sub>1</sub> - C(CH <sub>2</sub> )CH <sub>2</sub> CC <sub>1</sub> H <sub>3</sub> · CH <sub>1</sub> · CCH <sub>3</sub> CH <sub>4</sub> CC <sub>1</sub> H <sub>3</sub> · CH <sub>1</sub> · CCH <sub>3</sub> CH <sub>4</sub> CC <sub>1</sub> H <sub>3</sub> · CH <sub>1</sub> · CCH <sub>3</sub> CH <sub>4</sub> CH <sub>4</sub> · oc)CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> · CCH <sub>3</sub> · CCH <sub>3</sub> CH <sub>4</sub> CH <sub>4</sub> · oc)CC <sub>1</sub> CH <sub>3</sub> · oc)CCH <sub>3</sub> · CCH <sub>3</sub> · oc)CCH <sub>3</sub> ·	1111	NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub>	Ethanol Ethanol Ethanol Ethanol	######################################
	C3 r:C3H11X\$ r:C3H1CH(CH3)X\$	СП <sub>2</sub> - ((СП <sub>2</sub> )СП <sub>4</sub> (СО <sub>3</sub> П <sub>11</sub> -т)СО <sub>3</sub> СП <sub>3</sub> ); СП <sub>2</sub> - ((СП <sub>3</sub> )СП <sub>4</sub> (СО <sub>3</sub> П <sub>11</sub> -т)СО <sub>3</sub> СП <sub>3</sub> );	1 1	NaOC <sub>4</sub> II <sub>5</sub> NaOC <sub>4</sub> II <sub>5</sub>	Ethanol Ethanol	51 51 52 52 54 52
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	2.Chloromethy Ithlophens	$\operatorname{CH}_{1^{-1}}(\mathbb{C}(\mathbb{C}\Pi_{1})\mathbb{C}\Pi_{2}\mathbb{C}(\mathbb{C}\Pi_{1}\mathbb{C}_{1}\Pi_{3}\mathbb{S})(\mathbb{C}O_{1}\mathbb{C}_{1}\Pi_{3})_{1}$	1	Na	None	897
	C4 n-C <sub>4</sub> H <sub>13</sub> X; (C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> CHCH <sub>4</sub> X;	$CH_{1} - C(CH_{3})CH_{1}C(C_{4}H_{13},n)CO_{1}C_{2}H_{3})_{1}$ $CH_{1} - C(CH_{3})CH_{1}C(C_{4}H_{13},n)CO_{1}C_{2}H_{3})_{2}$	11	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	Ethanol Ethanol	552 552
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	$^{n-C_5H_{11}C(C_4H_7)(CO_2C_2H_5)_2}$	n-C <sub>2</sub> H <sub>1</sub> aC(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>2</sub> H <sub>1</sub> aC(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>3</sub> H <sub>1</sub> aC(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>3</sub> H <sub>1</sub> aC(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>1</sub> H <sub>1</sub> aC(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>1</sub> H <sub>2</sub> aC(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>1</sub> H <sub>3</sub> aC(C <sub>2</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>1</sub> H <sub>3</sub> aC(C <sub>2</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>1</sub> H <sub>3</sub> aC(C <sub>2</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>1</sub> H <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> S)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>1</sub> H <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> S)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>1</sub> H <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> S)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> c <sub>2</sub> H <sub>3</sub> C(C <sub>1</sub> H <sub>2</sub> S)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Dethyl evelopentyl-(2-thlenyl)malonate n-C <sub>4</sub> H <sub>3</sub> CC(H <sub>3</sub> S)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Dethyl evelopentyl-(2-thlenyl)malonate n-C <sub>4</sub> H <sub>3</sub> CC(H <sub>3</sub> S)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Dethyl evelohexyl-(2-thlenyl)malonate n-C <sub>4</sub> H <sub>3</sub> CC(H <sub>3</sub> S)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Diethyl evelohexyl-(2-thlenyl)malonate n-C <sub>4</sub> H <sub>3</sub> CC(1,1,2)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Diethyl evelohexyl-(2-thlenyl)malonate	
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		r r4de chloride lophene lophene smlde mide	
Cs-C14	n-C <sub>5</sub> H <sub>11</sub> Br	n-C <sub>6</sub> H <sub>13</sub> Br n-C <sub>7</sub> H <sub>15</sub> Br n-C <sub>9</sub> H <sub>15</sub> Br n-C <sub>9</sub> H <sub>15</sub> Br n-C <sub>9</sub> H <sub>15</sub> Br n-C <sub>1</sub> H <sub>2</sub> Br C <sub>1</sub> -C <sub>7</sub> CH <sub>3</sub> I C <sub>2</sub> H <sub>3</sub> I C <sub>3</sub> H <sub>4</sub> I C <sub>4</sub> CH <sub>2</sub> CI C <sub>4</sub> H <sub>5</sub> I C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>6</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>6</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub> C <sub>5</sub> H <sub>5</sub> I C <sub>7</sub> C <sub>5</sub>	
	κ	n-C <sub>6</sub> H <sub>11</sub> n-C <sub>6</sub> H <sub>11</sub> n-C <sub>6</sub> H <sub>11</sub> n-C <sub>6</sub> H <sub>11</sub> n-C <sub>1</sub> H <sub>2</sub> C <sub>1</sub> -C <sub>7</sub> C <sub>1</sub> H <sub>2</sub> C <sub>2</sub> H <sub>3</sub> n-C <sub>2</sub> H <sub>3</sub> n-C <sub>2</sub> H <sub>3</sub> n-C <sub>3</sub> H <sub>3</sub> n-C <sub>3</sub> H <sub>3</sub> n-C <sub>3</sub> H <sub>3</sub> C <sub>1</sub> H <sub>2</sub> C <sub>1</sub> H <sub>2</sub> C <sub>1</sub> H <sub>2</sub> C <sub>2</sub> H <sub>3</sub> n-C <sub>4</sub> H <sub>3</sub> C <sub>1</sub> H <sub>2</sub> C <sub>1</sub> H <sub>2</sub> C <sub>1</sub> H <sub>2</sub> C <sub>1</sub> H <sub>2</sub> n-C <sub>4</sub> H <sub>3</sub> n-C <sub>4</sub> n-C <sub>4</sub> H <sub>3</sub> n-C <sub>4</sub> n	
<b>.</b> .	> сиси <sub>2</sub> си <sub>2</sub> == С <sub>4</sub> п,)	n-C <sub>6</sub> H <sub>13</sub> Br n-C <sub>5</sub> H <sub>15</sub> Br n-C <sub>9</sub> H <sub>13</sub> Br n-C <sub>9</sub> H <sub>13</sub> Br n-C <sub>9</sub> H <sub>13</sub> Br n-C <sub>1</sub> H <sub>2</sub> Br C <sub>1</sub> -C <sub>7</sub> C <sub>1</sub> H <sub>2</sub> C <sub>1</sub> H <sub>2</sub> C <sub>2</sub> H <sub>3</sub> C <sub>2</sub> H <sub>3</sub> I C <sub>1</sub> H <sub>2</sub> CI C <sub>2</sub> H <sub>3</sub> Br C <sub>1</sub> C <sub>2</sub> H <sub>3</sub> Br n-C <sub>3</sub> H <sub>3</sub> Br C <sub>3</sub> Clotomyyl bromide 2-Cyclopentyl bromide 3-Cyclohexyl bromide 2-Cyclohexyl bromide 3-Cyclohexyl	
CH		C <sub>2</sub> H <sub>5</sub> C  2-Tiulen  2-Tiulen  4 The ha	

## TABLE III—Continued

Alkylation of Monoalkylmalonic Esters,  $R{\rm 'CH(CO_2R)_2}$ (The diothyl ester was used unless otherwise indicated.)

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Yield,   (The di	(The dietnyl ester was used anno				Refer-	
	Alkylating Agent	Product	Yleld, %	Basc	Solvent	enec
H <sub>2</sub>  C	C <sub>2</sub> C <sub>2</sub> H <sub>3</sub> Br BrOH <sub>2</sub> CH <sub>2</sub> Br	$n \cdot c_5 H_{11} C(c_2 H_5) (CO_3 C_2 H_5)_3$ $(CH_2)_2 C(c_5 H_{11} \cdot n) CO_2 C_2 \Pi_5$ 0 CO	40	NaOC <sub>2</sub> H <sub>5</sub> Na	Ethanol $C_6H_6$	148 555
H <sub>2</sub>  C	C <sub>3</sub> CH <sub>3</sub> SCH(CH <sub>3</sub> )Cl CH <sub>4</sub> =CHCH <sub>2</sub> Br Br(CH <sub>2</sub> )Br	$CH_3 SCH(CH_3) C(C_3 H_{11} \cdot n) (CO_2 C_2 H_3)_2$ $CH_3 = CHCH_3 C(C_3 H_{11} \cdot n) (CO_2 C_2 H_3)_2$ $DH(CH_2)_2 C(C_3 H_{11} \cdot n) (CO_2 C_2 H_3)_2$	70-90	NaOC <sub>2</sub> H <sub>6</sub> NaOC <sub>2</sub> H <sub>5</sub> Na	Toluenc Ethanol —	126 545, 743 656
(C <sub>5</sub> II <sub>11</sub> -n) <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> n-C <sub>6</sub> II <sub>12</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> n-C <sub>5</sub> II <sub>13</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> None  n-C <sub>5</sub> H <sub>17</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> n-C <sub>5</sub> H <sub>17</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> n-C <sub>5</sub> H <sub>17</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> nationate  nationate  n-C <sub>5</sub> II <sub>10</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> nationate  n-C <sub>5</sub> II <sub>10</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> nationate  n-C <sub>5</sub> II <sub>10</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> nationate  n-C <sub>5</sub> II <sub>10</sub> C(C <sub>5</sub> II <sub>11</sub> -n)(CO <sub>5</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> nationate	<i>C</i> ₄ C₄II,SCII(CII,3)Ci i÷C₄II,9Dr	$C_{2,\Pi,S}\text{CH}(\text{CH}_3)\text{CC}_3\Pi_{11}\text{-BM}(\text{CO}_2\text{C}_2\Pi_5)_2\\ n\text{-C}_3\Pi_{11}\text{CC}_4\Pi_9\text{-1}\text{N}(\text{CO}_2\text{C}_4\Pi_5)_2$	70-90 70-85	NaOC2H5 NaOC2H5	Toluene Ethanol	126 545
hexylcthyl bromide Dictinyl n-amyl-(h-cyclohexylethyl)- hexylpropyl bromide Diethyl n-amyl-(r-cyclohexylpropyl)- malonate malonate n-c <sub>0</sub> lf <sub>10</sub> C(c <sub>2</sub> H <sub>11</sub> ,n)(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-c <sub>0</sub> lf <sub>10</sub> C(c <sub>3</sub> H <sub>11</sub> ,n)(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-c <sub>0</sub> lf <sub>10</sub> C(c <sub>3</sub> H <sub>11</sub> ,n)(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-c <sub>0</sub> lf <sub>10</sub> C(c <sub>3</sub> H <sub>11</sub> ,n)(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-c <sub>0</sub> lf <sub>10</sub> C(c <sub>3</sub> H <sub>11</sub> ,n)(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-c <sub>0</sub> lf <sub>10</sub> C(c <sub>3</sub> H <sub>11</sub> ,n)(Co <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	C <sub>5</sub> -C <sub>7</sub> n-C <sub>5</sub> H <sub>11</sub> Br n-C <sub>7</sub> H <sub>13</sub> Br n-C <sub>7</sub> H <sub>13</sub> Br CH <sub>3</sub> CHBr(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	(C <sub>5</sub> II <sub>11</sub> ·n) <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> II <sub>2</sub> ) <sub>2</sub> n·C <sub>6</sub> II <sub>12</sub> C(C <sub>5</sub> II <sub>11</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> n·C <sub>7</sub> II <sub>15</sub> C(C <sub>5</sub> II <sub>11</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> None	1111	NaOC2Hs NaOC2H5 NaOC2H5 NaOC2H5	Ethanol Ethanol Ethanol Ethanol	641 641 641 720
malonate Diethyl n-amy-t/c-cyclohexylpropyl)- malonate n-C <sub>0</sub> II <sub>10</sub> C(C <sub>0</sub> I <sub>11</sub> n)(CO <sub>2</sub> C <sub>2</sub> I <sub>3</sub> ) <sub>2</sub> Diethyl n-amyl-(∂-cyclohexylbutyl)- malonate	$C_8-C_{16}$ $n\cdot C_8\Pi_{17}X_{\div}^*$ $eta\cdot C_8$ clohexylethyl bromide	$n\cdot C_6H_1 \cdot C(C_5H_{11} \cdot n)(CO_2C_2H_5)_2$ Dictiyl $n\cdot amyl\cdot (\beta\cdot cyclohexylethyl)$ -	1.1	NaOC <sub>2</sub> U <sub>5</sub> NaOC <sub>2</sub> U <sub>5</sub>	Ethanol Ethanol	887 902
malonate $n\text{-}\text{C}_0 \text{II}_1 \text{O}(\text{C}_0 \text{II}_1 n) (\text{CO}_2 \text{C}_2 \text{H}_2)_2$ — Vibutyi bromide Diethyi $n\text{-}\text{anyl-}(\text{-}\text{eyclohexylbutyi})$ . — $n\text{-}\text{malonate}$	7-Cyclohexylpropyl bromide	malonate Diethyl n-amyl-(y-cyclohexylpropyl)-	ţ	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	302
Illustonave	$n\text{-}\mathrm{C}_{\mathfrak{g}}\mathrm{H}_{1\mathfrak{g}}\mathrm{Br}$ 3-Cyclohexylbutyl bromíde	malonate n-C <sub>0</sub> II <sub>10</sub> C(C <sub>2</sub> H <sub>11</sub> n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> DlethyI n-amyl-(d-cyclohexylbutyI)- malonate	1.1	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>6</sub>	Ethanol Ethanol	888 902

	THE REKIEKTION	OF ESTERS AN	D MITRILES
387 888 920 887 135	532 35 890 316 555, 316	282 718 125 556 556 537	553 203 545 916 11
Ethanol Ethanol Ethanol Ethanol	Ethanol  CC4HgOH  (C2H5O)2CO C6H6 C6H6 C6H6 Ethanol	Ethanol Ethanol Toluene Ether Ethanol G, II,	Toluene C <sub>6</sub> H <sub>6</sub> -ether Ethanol Ethanol
$NaOC_2H_5$ $NaOC_2H_5$ $NaOC_2H_5$ $NaOC_2H_5$ $NaOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>4</sub> H <sub>9</sub> -1 NaOC <sub>2</sub> H <sub>8</sub> Na Na Na Na Na NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> Na NaOC <sub>2</sub> H <sub>5</sub> Na NaOC <sub>2</sub> H <sub>5</sub> Na	NaOC <sub>2</sub> H <sub>5</sub> NaNH <sub>2</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>
11112	86 78 45 (60)§ — 85–90	Ca. 70	70-90 63 70-85 70
n-C <sub>10</sub> H <sub>21</sub> C(C <sub>5</sub> H <sub>11</sub> -n)(CO <sub>5</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>11</sub> H <sub>32</sub> C(C <sub>5</sub> U <sub>11</sub> n)(CO <sub>5</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyl n-amyl-(n-undecenyl)malonate n-C <sub>12</sub> H <sub>22</sub> C(C <sub>5</sub> U <sub>11</sub> -n)(CO <sub>5</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>16</sub> H <sub>33</sub> C(C <sub>5</sub> H <sub>11</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	i-C <sub>5</sub> H <sub>11</sub> C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> i-C <sub>5</sub> H <sub>11</sub> C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> i-C <sub>5</sub> H <sub>11</sub> C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>1</sub> -1)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>11</sub> -1)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> )	CH2,2CH(C3,H1-1)  0—C0  c2,H1,C(C3,H1-1)  C2,H2,C(H2,C(C3,H1-1))  C2,H2,C(M2,M2,H1-1)  C2,H3,C(M2,M2,H1-1)  CH3,2C(M2,M2,H1-1)  HC=CH2,4C(C4,H1-1)(CO2,C3,H3,2)  BACH2,4C(C4,H1-1)(CO2,C3,H3,2)	$\begin{array}{c} C_2 H_5 \mathrm{S}(\mathrm{CH}_2)_2 \mathrm{C}(\mathbf{c}_5 H_{11} \cdot \mathbf{i}) (\mathrm{CO}_2 C_3 H_2)_2 \\ C_2 H_3 \mathrm{O} \mathrm{CH}(\mathrm{CH}_3) \mathrm{C}(\mathbf{c}_5 H_{11} \cdot \mathbf{i}) (\mathrm{CO}_2 C_2 H_2)_2 \\ \mathbf{i} \cdot C_2 H_{11} \mathrm{C}(\mathbf{c}_4 H_2 \cdot \mathbf{i}) \mathrm{CO}_2 C_3 H_3)_2 \\ \mathrm{CH}_3 \mathrm{CG} = \mathrm{CH} \mathrm{CH}_2 \mathrm{C}(\mathbf{c}_5 H_1 \cdot \mathbf{i}) \mathrm{CO}_2 C_2 H_3)_2 \\ \mathrm{CH}_2 = \mathrm{CH} \mathrm{CH} \mathrm{GH}_2 \mathrm{C}(\mathbf{c}_5 H_{11} \cdot \mathbf{i}) \mathrm{CO}_2 C_2 H_3 \\ \mathrm{CH}_2 = \mathrm{CH} \mathrm{CH} \mathrm{CH}_2 \mathrm{C}(\mathbf{c}_5 H_{11} \cdot \mathbf{i}) \mathrm{CO}_2 C_2 H_3 \\ \mathrm{CH}_2 = \mathrm{CH} \mathrm{CH} \mathrm{CH}_2 \mathrm{C}(\mathbf{c}_5 H_{11} \cdot \mathbf{i}) \mathrm{CO}_2 C_2 H_3 \end{array}$
n-C <sub>10</sub> H <sub>21</sub> X; n-C <sub>11</sub> H <sub>23</sub> X; n-Undecenyl bromide n-C <sub>12</sub> H <sub>25</sub> X; n-C <sub>16</sub> H <sub>33</sub> I	C <sub>2</sub> C <sub>2</sub> H <sub>2</sub> Dr C <sub>2</sub> H <sub>3</sub> X† (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO Ci(CH <sub>2</sub> ) <sub>2</sub> I Br(CH <sub>2</sub> ) <sub>2</sub> Br Br(CH <sub>2</sub> ) <sub>2</sub> Br	CH <sub>2</sub> —CH <sub>2</sub> C <sub>3</sub> C <sub>3</sub> C <sub>3</sub> H,Br C <sub>2</sub> H <sub>8</sub> SCH <sub>2</sub> Cl (CH <sub>2</sub> ) <sub>2</sub> CClNO <sub>2</sub> HC≡CCH <sub>2</sub> Br Dr(CH <sub>2</sub> ) <sub>3</sub> Br	$\begin{array}{c} C_4 \\ C_2 H_5 S (G H_2)_2 G \\ C_2 H_5 G G H (G H_3) G \\ i \cdot C_4 H_5 B r \\ C H_3 G C i = C H C H_2 G \\ C H_2 = C H C H - C H_2 \\ \end{array}$

Note: References 577-1080 are on pp. 322-331.

# The halogen was not specified.

§ Here and in subsequent cases the first figure represents the conversion; the figure in parentheses represents the yield.

TABLE III.-Contenued

MANUATOR OF MOROALKYPAMONIC ESTERS, RUCH(CO.R);

	Maxe.	Arkylation of Minimaria meeting (The definite militated)	s mdica	teel.)		•
£	Man'atha Arts	Pestuci	Yletd.	Baie	\$6 vent	rnee cnee
·  \( \text{H}_4 \cond \cond \( \text{T} \)	et et en	c <sub>1</sub> n <sub>1</sub> o <sub>1</sub> ccncunvec <sub>1</sub> n <sub>1</sub> ouco <sub>1</sub> c <sub>1</sub> n <sub>2</sub> , c <sub>1</sub> n <sub>2</sub> ocncunvec <sub>1</sub> n <sub>1</sub> ouco <sub>1</sub> n <sub>1</sub> s c <sub>1</sub> n <sub>2</sub> ocncun <sub>1</sub> n <sub>1</sub> oc <sub>1</sub> n <sub>1</sub> ouco <sub>1</sub> c <sub>2</sub> n <sub>2</sub> , c <sub>1</sub> n <sub>2</sub> ocncun <sub>2</sub> n <sub>2</sub> oc <sub>1</sub> n <sub>1</sub> ouco <sub>1</sub> c <sub>1</sub> n <sub>2</sub> , c <sub>1</sub> n <sub>2</sub> ocnun <sub>1</sub> n <sub>2</sub> oc <sub>1</sub> n <sub>1</sub> n <sub>2</sub> aco <sub>1</sub> n <sub>2</sub> ,	ត្រ ក្នុង	NaOC <sub>1</sub> II <sub>2</sub> Na NaOC <sub>1</sub> II <sub>2</sub> NaOC <sub>1</sub> II <sub>3</sub> NaOC <sub>1</sub> II <sub>3</sub> NaOC <sub>2</sub> II <sub>3</sub>	Ethanol None Ethanol Ethanol Ethanol	5 5 5 5 5 5 T T T T T T T T T T T T T T
हैं। है। एक एक	chi chansaha chisaha ansaha o	0 —— 0 0 —— 0 0 —— 0 0 11, correction particular of 1133 0 11, correction particular of 1133 0 11, correction of 1133	1111	N.1 N.10C <sub>2</sub> 11 <sub>5</sub> N.10C <sub>2</sub> 11 <sub>5</sub> N.20C <sub>2</sub> 11 <sub>5</sub>	Ether Toluene Toluene	658 125 125 125
	gette in merlij tiblopkene g Chemietrelij dropy ran	C <sub>1</sub> H <sub>2</sub> SCH <sub>4</sub> C{CHCH <sub>4</sub> NC <sub>4</sub> H <sub>7</sub> ·n Ordry (2-tetralrydropyrany)- (1-methylbaty))malonate	1 1	Na NaII	None Toluene	897
entenentan.	e, e, en, encurb	CH4- CHCH4C(CO4C4H4)4	70-85	NaOC <sub>2</sub> 11 <sub>2</sub>	Ethanol	919
	n-C <sub>11</sub> H <sub>11</sub> N; n-C <sub>11</sub> H <sub>15</sub> N;	C11,CHCH3C11; C11,CHCH3CH4CC0,L11;20CO2C113); C11,CHCH3CH4CCO2C111;2	1 1	NaOC <sub>2</sub> II <sub>2</sub> NaOC <sub>2</sub> II <sub>5</sub>	Ethanof Ethanol	888
виме сиси	C <sub>1</sub> -C; C <sub>4</sub> H <sub>2</sub> X; n-C <sub>4</sub> H <sub>3</sub> X; n-C <sub>4</sub> H <sub>3</sub> X;	*(*n*5*03/k*n*3)*(*n3) - 5*(*n3) *(*n*5*03/k*n*3)*(*n3) - 5*(*n3) *(*n*5*03/k*n*3)*(*n3) - 5*(*n3)	65 80 Poor	NaOC <sub>3</sub> II, NaOC <sub>3</sub> II, NaOC <sub>2</sub> II,	(C <sub>4</sub> 11 <sub>4</sub> 0) <sub>2</sub> CO (C <sub>4</sub> 11 <sub>5</sub> 0) <sub>2</sub> CO Ethanol	063 063 912

	$CH_2 = CHCH_2Br$	$(CH_3)_2C = CHCII_2C(CO_2C_2II_5)_2$	11	NaOC <sub>2</sub> II <sub>5</sub>	Ethanol	912
	$n$ -C $_4$ H $_6$ X $_4$		85 65	NaOC <sub>2</sub> H <sub>s</sub> NaOC <sub>2</sub> H <sub>s</sub>	$(C_2H_5O)_2CO$ $(C_2H_5O)_2CO$	663 663
	$(CH_3)_2C = CHCH_2Br$ Not stated	$ ((CH_3)_2C = CHCH_2)_2C(CO_2C_2H_3)_2                                   $	80 80	NaOC2Hs NaOC2Hs	$(c_2H_50)_2C0$ $(c_2H_50)_2C0$	663 663
(CII <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> X‡ BrCH <sub>2</sub> ,PCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> BrCH <sub>2</sub> CHCH <sub>2</sub> CO <sub>2</sub> C <sub>4</sub> H <sub>5</sub>	(CH <sub>3</sub> )cC=CHCH <sub>2</sub> VCH <sub>2</sub> C <sub>6</sub> H <sub>3</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) (C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> CHCO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> CH(CO <sub>2</sub> CH <sub>3</sub> CH <sub>2</sub> C- (CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub>	25 55	NaOC2H5 NaOC2H5 NaOC2H5	(C <sub>2</sub> tt <sub>5</sub> C) <sub>2</sub> CO Ethanol Ethanol	670 671
CH(CH <sub>3</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub> 1 C <sub>2</sub> H <sub>3</sub> 1 C <sub>4</sub> H <sub>5</sub> CH <sub>2</sub> Cl	$\begin{array}{l} c_2H_2O_2CCH(CH_3)C(CH_3)CO_2C_2H_3)_2\\ c_2H_2O_2CCH(CH_3)C(C_2H_3)(CO_2C_3H_3)_2\\ c_2H_2O_2CCH(CH_3)C(CH_2C_3H_3)(CO_2C_2H_3)_2 \end{array}$	111	Na Na Na	None None None	161 162 923
	$C_2$ - $C_{11}$					
$Cyelopentyl(=C_5H_9)$	C,H,Br	C5H3C(C2H5)(CO2C2H5)2	48	NaOC2H3	Ethanol	148
	n-C,H15Br	$n \cdot C_7 H_{15} C(C_6 H_6) (CO_2 C_2 II_6)_2$	20-00	No	CeHe	752
	n-CaH17Br	n-CgH1,C(CgH9)(CO2C2H5)2	20-00	Na	Con	725
	n-CoHisBr	n-C,111,9C(C,H,0)(CO,2C,H,5)2	20-60	Na	c, II,	795
	n-CloH21Br	n-C10H21C(C6H2)(CO2C2H5)2	20-00	Na	Con	725
	Geranyl bromide n-C, H, Br	Dicthyl eyelopentyl(geranyl)malonafe n-C.,H.,C(C,H.)(CO,C,H.),	25 50-60	NaOC <sub>2</sub> H <sub>S</sub> Na	Ethanol C.H.	38. 28.
	i ; °	1.0.2.7.1.2.7.7	:			ì
2-Cyclopentenyl	$C_2H_5B_\Gamma$	$C_5 \Pi_7 C(C_2 \Pi_5) (CO_2 \Pi)_2$	30	Na	Toluene	151
(=: 0gm2)	$n$ - $C_3H_7Br$	$C_5\Pi_7C(C_3\Pi_7\cdot n)(CO_2H)_2$	20	Na	Toluene	151
	i-C <sub>3</sub> H,Br	C <sub>6</sub> H <sub>7</sub> C(C <sub>3</sub> H <sub>7</sub> -i)(CO <sub>2</sub> H) <sub>2</sub>	80	Na	Toluene	151
	$CH_2 = CIICH_2Br$	$CII_2 = CHCH_2C(C_5H_7)(CO_2\Pi)_2$	33	Na	Toluene	151
	n-C4H9Br	$n\text{-}\mathrm{C}_4\mathrm{H}_{\mathfrak{g}}\mathrm{C}(\mathrm{G}_5\mathrm{H}_7)(\mathrm{CO}_2\mathrm{H})_{2}$	35	Na	Toluene	151
	n-C <sub>5</sub> H <sub>11</sub> Br	$n$ - $C_5H_{11}C(C_6H_7)(CO_2C_2H_5)_2$	37	NaOC <sub>2</sub> H <sub>6</sub>	Ethanol	089
	z-Cyclopenienyi ellioriae	(C <sub>5</sub> H <sub>2</sub> ) <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	20	Na	Toluene	151, 925,
Note: References	Note: References 577-1080 are on pp. 322-331.					926

Note: References 577-1080 are on pp. 322-331. ‡ The halogen was not specified.

## TABLE III-Continued

Alkylation of Monoalkylmalonic Estens,  $\mathrm{R}^*\mathrm{CH}(\mathrm{CO}_2\mathrm{R})_2$ 

Š	Heler- ence	223 223 223 223 11	658 125 125 125	807 683	545	888	003 003 912
	Solvent	Ethanol None Ethanol Ethanol Ethanol	Ether Toluene Toluene Toluene	None Tolucne	Ethanol	Ethanol Ethanol	02°(0°H°2) 02°(0°H°2) 03°(0°H°2)
nted.)	Ваяс	NAOC <sub>2</sub> II <sub>3</sub> NA NAOC <sub>2</sub> II <sub>5</sub> NAOC <sub>2</sub> II <sub>5</sub> NAOC <sub>2</sub> II <sub>5</sub>	Nn NnOC <sub>2</sub> H <sub>5</sub> NuOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Na Naff	NaOC <sub>2</sub> II <sub>5</sub>	$NaOC_2 H_5$ $NaOC_2 H_5$	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>
so indic	Yleid,	24 0 11 Poor	1111	11	70-85	1.1	65 80 Poor
(The diethyl ester was used unless otherwise indicated.)	Product	C <sub>1</sub> H <sub>2</sub> O <sub>2</sub> CCHCH <sub>2</sub> CC <sub>3</sub> H <sub>11</sub> -3)(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>1</sub> H <sub>3</sub> O <sub>2</sub> CCH(C <sub>3</sub> H <sub>3</sub> )CC <sub>3</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>3</sub> H <sub>3</sub> O <sub>2</sub> CCH(C <sub>4</sub> H <sub>3</sub> )CC <sub>4</sub> H <sub>4</sub> -3)(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>3</sub> H <sub>3</sub> O <sub>3</sub> CCH(C <sub>3</sub> H <sub>2</sub> -3)CC <sub>4</sub> H <sub>4</sub> -3)(CO <sub>3</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>3</sub> C <sub>3</sub> H <sub>3</sub> O <sub>4</sub> CCH(C <sub>3</sub> H <sub>2</sub> -3)CC <sub>4</sub> H <sub>3</sub> -3)(CO <sub>3</sub> C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub>	$\begin{array}{l} 0 &   \cup \\ 0 &   \cup \\ \text{Cell}_{2}\text{CoCH}_{2}\text{Cr}_{3}\text{H}_{11}^{-3}\text{NCO}_{2}\text{C}_{2}\text{H}_{3})_{2} \\ \text{Cell}_{2}\text{SCH}_{2}\text{ClCH(CH}_{2}\text{NC}_{4}\text{H}_{7}^{-3}\text{NCO}_{2}\text{C}_{2}\text{H}_{3})_{2} \\ \text{Cell}_{2}\text{SCH}_{2}\text{ClCH(CH}_{3}\text{NC}_{4}\text{H}_{7}^{-3}\text{NCO}_{2}\text{C}_{2}\text{H}_{3})_{2} \\ \text{Cell}_{2}\text{CCH}_{2}\text{ClCH}_{3}\text{ClC}_{2}\text{Co}_{3}\text{C}_{3}\text{H}_{3})_{2} \end{array}$	C1H_SCH_C[CH(CH_3)C_3H_7-n]CO_2C_3H_5)z Dlethyl 2-tetralydropyranyl- (1-methylbutyl)maionate	$\mathrm{CH}_{\mathbf{i}} = \mathrm{CHCH}_{\mathbf{i}} \mathrm{C}(\mathrm{CO}_{\mathbf{i}} \mathrm{C}_{\mathbf{i}} \mathrm{H}_{\mathbf{i}})_{\mathbf{i}}$	C <sub>2</sub> H <sub>2</sub> CH(CH <sub>3</sub> )C <sub>2</sub> H <sub>3</sub> C <sub>2</sub> H <sub>2</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> C(C <sub>10</sub> H <sub>21</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>1</sub> H <sub>3</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	$(CH_{1})_{1}C = CHCH_{2}C(C_{1}H_{2})^{*}(CO_{2}C_{2}H_{3})_{2}$ $(CH_{1})_{2}C = CHCH_{2}C(C_{3}H_{7})^{*}(CO_{2}C_{2}H_{3})_{3}$ $(CH_{1})_{2}C = CHCH_{2}C(C_{3}H_{7})^{*}(CO_{2}C_{3}H_{3})_{3}$
AERYEA (The	Alkylating Agent	C <sub>3</sub> -C <sub>3</sub> -C <sub>3</sub> -C <sub>4</sub> -C <sub>1</sub>	C4,11,5C11,C1 C4,11,5C11,C1 C4,11,5C11,C1 C4,11,5C11,C1	2-ChloromethyRhlophene 2-Chlorotetrahydropyran	$C_{\mathbf{i}}^{-C_{\mathbf{i}}\mathbf{z}}$ (TII <sub>2</sub> := CHCII <sub>2</sub> IB:	n-C <sub>10</sub> H <sub>33</sub> X* n-C <sub>12</sub> H <sub>33</sub> X*	C4-C; C4H;X; n-C4H;X; i-C4H;W
	<u>بر</u>	r¢,44, (Cont.)	n-C <sub>3</sub> H <sub>2</sub> CH(CH <sub>3</sub> )		c, II, CII(CII, )CII,		(CH)}c=CHCH,

					MD MI	TIMES
913	663 663 663	603 670 671	101 162 923	21. 25. 25. 25. 25. 25. 25. 25. 25. 25. 25.	151	151 151 151 151 151 151, 925, 926
Ethanol	(C <sub>2</sub> H <sub>3</sub> O) <sub>2</sub> CO (C <sub>2</sub> H <sub>3</sub> O) <sub>2</sub> CO (C <sub>2</sub> H <sub>3</sub> O) <sub>2</sub> CO	(C <sub>2</sub> H <sub>3</sub> O) <sub>2</sub> CO (C <sub>2</sub> H <sub>3</sub> O) <sub>2</sub> CO Ethanol Ethanol	None None None	Ethanol C <sub>4</sub> H <sub>8</sub> C <sub>4</sub> H <sub>8</sub> C <sub>4</sub> H <sub>8</sub> C <sub>6</sub> H <sub>8</sub> C <sub>6</sub> H <sub>8</sub> C <sub>6</sub> H <sub>8</sub> Ethanol	Toluene	Toluene Toluene Toluene Toluene Ethanol Toluene
NaOC <sub>2</sub> II <sub>3</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub> NaOC <sub>2</sub> H <sub>3</sub>	N N N N N	NaOC <sub>2</sub> H <sub>3</sub> Na Na Na Na Na Na NaOC <sub>2</sub> H <sub>3</sub>	Na	Na Na Na NaOC <sub>2</sub> II <sub>5</sub>
7.1	85 65 80 65	85 71 55	111	48 50-60 50-60 50-60 25 25	30	26 32 37 50
$(\mathrm{CH}_3)_2 \mathrm{C} = \mathrm{CH}_{\mathrm{CH}_1} \mathrm{C}_1^{\mathrm{C}} (\mathrm{CO}_2 \mathrm{C}_2 \mathrm{H}_5)_2$	$\begin{array}{l} \mathrm{CH}_{2}\mathrm{CH}_{2}\mathrm{CH} = \mathrm{CH}_{2} \\ \mathrm{CH}_{13}\mathrm{C} = \mathrm{CHCH}_{2}\mathrm{C(C}_{11}\mathrm{G}_{7}\mathrm{-3})\mathrm{K}\mathrm{Co}_{2}\mathrm{C}_{11}\mathrm{J}_{3} \\ \mathrm{CH}_{3)}\mathrm{G} = \mathrm{CHCH}_{2}\mathrm{C(C}_{11}\mathrm{G}_{7}\mathrm{-3}\mathrm{K}\mathrm{Co}_{2}\mathrm{G}_{2}\mathrm{J}_{13}\mathrm{J}_{2} \\ \mathrm{(CH}_{3)}\mathrm{C} = \mathrm{CHCH}_{2}\mathrm{L}\mathrm{C(Co}_{2}\mathrm{G}_{2}\mathrm{H}_{3}\mathrm{J}_{2} \\ \mathrm{CH}_{3}\mathrm{L}\mathrm{C} = \mathrm{CHCH}_{2}\mathrm{L}\mathrm{C(Co}_{2}\mathrm{G}_{2}\mathrm{H}_{3}\mathrm{J}_{2} \\ \mathrm{CH}_{3}\mathrm{L}\mathrm{C} = \mathrm{CHCH}_{2}\mathrm{C(C}_{6}\mathrm{H}_{1}\mathrm{-cyclo)(Co}_{2}\mathrm{C}_{2}\mathrm{H}_{3}\mathrm{J}_{2} \\ \end{array}$	(CH <sub>3</sub> ) <sub>2</sub> C=CHCH <sub>2</sub> (C <sub>6</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> CH <sub>2</sub> O <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>3</sub> O <sub>3</sub> CCH <sub>2</sub> CH <sub>2</sub> O <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> (CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>3</sub> (CH <sub>2</sub> C <sub>2</sub> C <sub>2</sub> H <sub>3</sub>	$\begin{array}{l} C_2\Pi_3O_2CC\Pi(C\Pi_3)C(C\Pi_3)C(O_2C_2\Pi_3)_2 \\ C_3\Pi_3O_2CC\Pi(C\Pi_3)C(C_2\Pi_3)(CO_2C_2\Pi_3)_2 \\ C_2\Pi_3O_2CC\Pi(C\Pi_3)C(C\Pi_2C_3\Pi_3)(CO_2C_2\Pi_3)_2 \end{array}$	C <sub>3</sub> H <sub>2</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ), n-C <sub>3</sub> H <sub>3</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ), n-C <sub>3</sub> H <sub>3</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ), n-C <sub>3</sub> H <sub>3</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ), n-C <sub>10</sub> H <sub>3</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ), Dichiyl cyclopentyl(geranyl)maionate n-C <sub>11</sub> H <sub>32</sub> C(C <sub>3</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ),	C,H,C(C,H,3)(CO,H),	$\begin{array}{l} C_{5}^{1} \Gamma_{1}^{1} C(C_{2}^{1} \Pi)_{2} \\ C_{5}^{1} \Gamma_{2}^{1} C(C_{5}^{1} \Pi_{1}^{1}) C(C_{2}^{1} \Pi)_{2} \\ C\Pi_{4} = C\Pi C\Pi_{4}^{2} C(C_{3}^{1} \Pi_{7}^{1}) C(C_{2}^{1} \Pi_{7}^{1}) \\ n \cdot C_{4}^{1} \Pi_{5}^{1} C(C_{5}^{1} \Pi_{7}^{1}) C(C_{5}^{1} \Pi_{7}^{1}) \\ (C_{5}^{1} \Pi_{1}^{1}) C(C_{5}^{1} C_{5}^{1} \Pi_{5}^{1})_{2} \end{array}$
CII3=CIICII2Br	n-C <sub>4</sub> H <sub>9</sub> N; sec-C <sub>4</sub> H <sub>5</sub> N; (CH <sub>5</sub> ) <sub>4</sub> C=CHOH <sub>2</sub> Br of H CH N+	Dr(CH2)2C02C2H3 BrCH2CH2CH2CO2C2H3 CO.C.H3	CH <sub>3</sub> I C <sub>4</sub> H <sub>5</sub> Cl C <sub>6</sub> H <sub>5</sub> Cl <sub>2</sub> Cl	C <sub>2</sub> H <sub>5</sub> Br n-C <sub>2</sub> H <sub>13</sub> Br n-C <sub>3</sub> H <sub>13</sub> Br n-C <sub>3</sub> H <sub>13</sub> Br n-C <sub>1</sub> H <sub>2</sub> Br n-C <sub>1</sub> H <sub>2</sub> Br	$c_2$ - $c_3$ $c_2$ H <sub>3</sub> Br $n$ - $c_3$ H, Br	i-C <sub>3</sub> $II_T^{BL}$ $CII_2 = CHCII_2Br$ $n-C_4II_3Br$ $n-C_3II_1Br$ $2-Cyclopentenyl ehlorlde$ Note: References 577–1080 are on pp. 322–331. The halogen was not specified.
		$(\mathrm{CH}_2)_2\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5$	сп(сп,)со,с,п,	$\mathrm{Cyclopentyl}(=\mathrm{C}_{\mathfrak{g}}\mathrm{H}_{\mathfrak{g}})$	2.Cyclopentenyi $(=C_3H_7)$	i·C <sub>3</sub> H <sub>2</sub> H <sub>3</sub> CH <sub>z</sub> =CI n·C <sub>4</sub> H <sub>3</sub> B n·C <sub>5</sub> H <sub>1</sub> P 2-Cyclope Note: References 577-1080 ar ‡ The halogen was not specified.

TABLE III-Continued

Alkylation of Monoalkylmalonic Esters,  $\mathrm{R'CH}(\mathrm{CO}_2\mathrm{R})_2$ (The diethyl ester was used unless otherwise indicated.)

Dofor-	cuco	080	720	080 080 014	080 028 31 928 928	679 287	082	350
	Solvent	Ethanol Xylene	Toluenc	Ethanol Tolueno Ethanol Xylene	Ethanol Ethanol Ethanol Ethanol	Xylene Toluene	Ethanol	Ethanol
	Baso	NaOC <sub>2</sub> H <sub>5</sub> Na	$NnOC_2U_5$	NaOC <sub>2</sub> U <sub>5</sub> Na NaOC <sub>2</sub> U <sub>5</sub> Na	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>6</sub> NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	Na Na K	NaOC <sub>2</sub> II <sub>5</sub>	$ m NaOC_2 H_5$
	Yleld, %	39 10	53	35 34 50	42 66-69 30 66-69	04 30	36	40
The dietayl ester was used united ourse	Product	\(\(\frac{1}{2}\)\(\f	$\begin{cases} c_{\delta}H_{\gamma} & c_{\delta}H_{\gamma} \\ Dlethyl 2-cycloliexenyl-(2-cyclopentenyl)- \\ \dots dracts \end{cases}$	n-C,II <sub>1</sub> ,C(C <sub>5</sub> II <sub>1</sub> )CO <sub>5</sub> C <sub>2</sub> II <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> II <sub>1</sub> ,CII <sub>2</sub> C(C <sub>5</sub> II <sub>1</sub> ,XCO <sub>5</sub> C <sub>2</sub> II <sub>3</sub> ) <sub>2</sub> n-C <sub>6</sub> II <sub>1</sub> ,XCO <sub>5</sub> I <sub>2</sub> II <sub>3</sub> ) <sub>3</sub> n-C <sub>6</sub> II <sub>1</sub> ,XCO <sub>5</sub> C <sub>2</sub> II <sub>5</sub> (C <sub>5</sub> II <sub>7</sub> XCO <sub>5</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub>	n-C <sub>9</sub> 1I <sub>19</sub> C(C <sub>9</sub> II <sub>2</sub> )(CO <sub>9</sub> C <sub>2</sub> II <sub>4</sub> ) <sub>2</sub> n-C <sub>10</sub> II <sub>12</sub> (C(C <sub>6</sub> II <sub>7</sub> )(CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub> ) <sub>2</sub> Dicthyl geranyl-(2-cyclopentenyl)malonate n-C <sub>11</sub> II <sub>12</sub> C(C <sub>6</sub> II <sub>7</sub> )(CO <sub>2</sub> C <sub>2</sub> II <sub>8</sub> ) <sub>2</sub>	n-C <sub>11</sub> I <sub>12</sub> C(C <sub>6</sub> II+)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> n-C <sub>16</sub> II <sub>2</sub> C(C <sub>6</sub> II+)(CO <sub>2</sub> C <sub>2</sub> H <sub>6</sub> ) <sub>2</sub> Dictivy I iva faocarpyi-(2-cyclopentenyl)- malonate	(CO CII2) 20(CO 2C2II5)2	o Jenzecozena)a
OHT.	Alkylating Agent	C <sub>6</sub> -C <sub>4</sub> n-C <sub>4</sub> -H <sub>13</sub> Dr Dr(CH <sub>2</sub> ) <sub>6</sub> Dr	1,2.Dibromocyclobexano	n-C,H,Br C,H,CH,CH n-C,H,Br n-C,H,Br	C <sub>p</sub> -C <sub>18</sub> n-C <sub>p</sub> H <sub>19</sub> Br n-C <sub>10</sub> H <sub>19</sub> Br Geranyl chlorido n-C <sub>11</sub> H <sub>23</sub> Br	n·C <sub>1,1</sub> H <sub>5,</sub> Br n·C <sub>1,6</sub> H <sub>3,9</sub> Br Hydnocarpyl bromlde-KI		cicii,co <sub>2</sub> c <sub>2</sub> ii,s
	<u>;</u> =	2-Cyclopentenyl (~C <sub>3</sub> H <sub>2</sub> ) (Cont.)					(.11)	CII.

$C_2$ - $C_6$ $C_1$ 113Br	C <sub>3</sub> H <sub>5</sub> SC(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> U <sub>5</sub> ) <sub>2</sub>	72	NaOC <sub>2</sub> H <sub>5</sub>	Bthanol	358
2-Cyclopentenyl chloride	Diethyl 2-eyelopentenyl-(2-thenyl)-	75	$Na0C_2H_5$	Ethanol	924
2-Chloromethytthiopheno 2-('yelohexenyl bromtka 6-2-(Thlonyl)ethyl etiloride	undionate (C <sub>6</sub> H <sub>8</sub> S) <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyl 2-cyclobexeny-(2-theny)malonate Diethylft-(2-thieny)bethyll-2-thenyl	121	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ethanol Ethanol Ethanol	50 924 50
C <sub>4</sub> 11 <sub>5</sub> CH <sub>2</sub> Cl p-Cyclohexystethyl broinkle	malonatu Gali,cH.Q(C <sub>4</sub> H <sub>3</sub> S)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> )2 Dictiyı (f.eyelohexylethyf)-2-thenyl- nalonate	1.1	NaOC <u>1</u> H5 NaOC <sub>2</sub> H5	Ethanol Ethanol	88
C <sub>2</sub> -C <sub>4</sub>	(UII,)2C(C4H,13-11)CO2C4H5	ca. 70	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	282
0 C, II, SCII, CI CII, = CHCH, Ik C, II, SCII(CII, ICI 2-Chloromethylthlophene n-C, II, Jr	0 — 60 C <sub>2</sub> II,SCII,Q(C <sub>6</sub> II <sub>13</sub> ,**)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> CII <sub>3</sub> =CIICII,C(C <sub>6</sub> II <sub>13</sub> **)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> II,SCII(CII <sub>3</sub> )C(C <sub>6</sub> II <sub>14</sub> **)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> C <sub>4</sub> II,SCII,C(C <sub>6</sub> II <sub>13</sub> ***)(CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> (C <sub>4</sub> II,****) <sub>2</sub> C(CO <sub>2</sub> C <sub>3</sub> II <sub>5</sub> ),	11-62	NaOC <sub>2</sub> H <sub>s</sub> NaOC <sub>2</sub> H <sub>s</sub> Na NaOC <sub>2</sub> H <sub>s</sub>	Toluene Toluene None Ethanol	125 743 126 897 641
C <sub>7</sub> -C <sub>9</sub> n-C <sub>7</sub> II <sub>13</sub> X; p-Cyclopentylethyl bromido	n-C <sub>7</sub> 1I <sub>16</sub> C(C <sub>6</sub> H <sub>13</sub> -n)(CO <sub>2</sub> C <sub>7</sub> H <sub>2</sub> ) <sub>2</sub> Dictityl n-lexyl-(\$-eyelopentylethyl)-	10-00	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Etlianol Etlianol	887 725
\$-(2-Cyclopentenyl)ethyl	malonate Dietlyl n-hexyl-[\beta-(2-eyelopentenyl)ethyl].	1	$NaOC_2H_5$	Ethanol	928
n-C <sub>8</sub> N <sub>11</sub> Nr n-C <sub>8</sub> N <sub>11</sub> Nr (i-Cyclohexylethyl bramide	natonne n-C <sub>3</sub> ll <sub>17</sub> C(C <sub>4</sub> ll <sub>13</sub> -n)(CO <sub>3</sub> C <sub>2</sub> ll <sub>5</sub> ) <sub>3</sub> Diethyl n-hexyl-(\$-eyclohexykelhyl)-	1.1	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ethanol Ethanol	888 902
n-C <sub>p</sub> H <sub>19</sub> X. 3-Cyclohexylpropyl bromide	natonate n-C <sub>2</sub> H <sub>19</sub> C(G <sub>4</sub> H <sub>13</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Diethyl n-hexyl-(r-cyclohexylpropyl)- malonate	1.1	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>6</sub>	Ethanol Ethanol	887 902

Note: References 577-1030 are on pp. 322-331, ‡ The halogen was not specified.

TABLE III—Continued

Alkylation of Monoalkylmalonic Esters,  $\mathrm{R'CH}(\mathrm{CO}_2\mathrm{R})_2$ (The diethyl ester was used unless otherwise indicated.)

Dofor.	ence	680	927	680 927 680 914	680 928 31 928 928 928 679	682	356
	Solvent	Ethanol Xylene	Toluene	Ethanol Toluene Ethanol Xylene	Ethanol Ethanol Ethanol Ethanol Ethanol Xylene Toluene	Ethanol	Ethanol
	Base	NaOC <sub>2</sub> H <sub>5</sub> Na	$NaOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub> Na NaOC <sub>2</sub> H <sub>5</sub> Na	, NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	$\rm NaOC_2H_5$	$NaOC_2H_5$
	Yield, %	39 10 22	53	35 07 34 50	42 66-69 30 66-69 66-89 64 36	36	40
ייים מוני דמפס ולוויים מודי	Product	$n_{C_0\Pi_{13}\mathrm{C}(C_0\Pi_7)(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2} \ / n_{\mathrm{C}(\Omega_{13})_6\mathrm{C}(C_0\Pi_7)(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2} \ / ((C_2\Pi_5)_{\mathrm{C}}(C_2\Pi_5)_{\mathrm{C}}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	$\begin{pmatrix} c_s H_{\gamma} & c_s H_{\gamma} \\ D$ lethyl 2-eyclohexenyl-(2-eyelopentenyl)-	malong n-c,H <sub>12</sub> QC <sub>0</sub> ,H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>4</sub> H <sub>2</sub> C(C <sub>2</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>3</sub> H <sub>1</sub> C(C <sub>3</sub> H <sub>2</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>4</sub> H <sub>3</sub> CH(C <sub>4</sub> U <sub>5</sub> )CH <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	n-C <sub>9</sub> H <sub>19</sub> C(C <sub>2</sub> H <sub>7</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>10</sub> H <sub>21</sub> C(C <sub>2</sub> H <sub>7</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Dickthyl germyl-(2-oyolopentonyl)malonate n-C <sub>11</sub> H <sub>13</sub> C(C <sub>3</sub> H <sub>7</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>12</sub> H <sub>13</sub> C(C <sub>3</sub> H <sub>7</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>16</sub> H <sub>13</sub> C(C <sub>3</sub> H <sub>7</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> n-C <sub>16</sub> H <sub>13</sub> C(C <sub>3</sub> H <sub>7</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> m-Dicktyl Hyduocarpyl-(2-cyolopentonyl)-malonate	$\left( \begin{bmatrix} & & & \\ & & & \\ & & & \end{bmatrix}_2 \text{C(CO}_2 \text{C}_2 \text{H}_5)_2 \right)$	CH2C(CO2C2H3)2
arr)	Alkylating Agent	$G_{\mathbf{d}} - G_{\mathfrak{g}}$ $n \cdot C_{\mathbf{d}} \coprod_{13} \mathrm{Br}$ $\mathrm{Br}(\mathrm{CH}_{2})_{\mathbf{d}} \mathrm{Br}$	1,2.Dlbromoeyclohexane	n-C,H,B C,H,CH,CI n-C,E1,Br n-C,H,CH(C,H,)CH,Br	C <sub>9</sub> -C <sub>16</sub> n-C <sub>9</sub> H <sub>19</sub> Br n-C <sub>10</sub> H <sub>21</sub> Br Geranyl chloride Granyl chloride n-C <sub>12</sub> H <sub>23</sub> Br n-C <sub>12</sub> H <sub>23</sub> Br n-C <sub>12</sub> H <sub>23</sub> Br Hydnocarpyl bromide-KI	CH <sub>2</sub> Br	$\mathrm{CiCH_2CO_2C_2H_5}$
	п,	2-Cyclopentenyl $(=C_bH_7)$ ( $Gom.$ )		•		CH2	$\left\lceil \begin{array}{c} \\ \\ \end{array} \right\rceil^{\operatorname{CH}_2}$

	THI	L ALK	YLATION	OF E	STERS	AND NITRILES	241
687 687 687 687	687 687 687	693	162 162 162	162 162	50, 708	35 743 926 32 50,709 32 147 149	32 719 32
1111	1111	I	None None None	None None	Ethanol	LC <sub>4</sub> H <sub>9</sub> OH  — — — Ethanol (C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CO Ethanol Toluene Ethanol	Ethanol Ethanol Ethanol
1111	1111	Na	Na Na Na	Na Na	$NaOC_2H_5$	NaOC <sub>4</sub> H <sub>9</sub> -t — — — — NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> Na Na Na	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>
1111	1111	77	111	1.1	Į.	58   1   68	15
$(C_2H_3)_2\mathrm{CHCH_2}(CG_3H_74)(\mathrm{CO}_2C_2H_3)_2\\ (C_2H_3)_2\mathrm{CHCH_2}(\mathrm{CCH}_4\mathrm{CH}=\mathrm{CH}_2)(\mathrm{CO}_2C_2H_3)_2\\ (C_2H_3)_2\mathrm{CHCH_2}(\mathrm{CCH}_2\mathrm{CH}=\mathrm{CH})(\mathrm{CO}_3C_3H_3)_2\\ (C_2H_3)_3\mathrm{CHCH_2}(\mathrm{CH}_2\mathrm{CH}=\mathrm{CH})(\mathrm{CO}_2C_3H_3)_2\\ \end{array}$	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CHCH <sub>2</sub> C(C <sub>4</sub> H <sub>5</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CHCH <sub>2</sub> C(C <sub>4</sub> H <sub>5</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> [(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CHCH <sub>2</sub> ] <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Diethyl 2-cyclohexenyl-(2-ethylbutyl).	cis- $C_2H_3\mathrm{CH}=\mathrm{CH}\mathrm{CH}_3)$ . $\mathrm{C}(\mathrm{CH}_3\mathrm{CH}=\mathrm{CH}_2)(\mathrm{CO}_2\mathrm{C}_2H_3)_2$	C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> CCH(C <sub>2</sub> H <sub>5</sub> )C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> CCH(C <sub>2</sub> H <sub>5</sub> )C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> CCH(C <sub>2</sub> H <sub>5</sub> )C(CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CC(CH <sub>3</sub> ) <sub>2</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CC(CH <sub>3</sub> ) <sub>2</sub> C(CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	C4H3S(CH2)AC(CH2SC4H3)(CO2C2H3)2	C <sub>6</sub> H <sub>11</sub> C(C <sub>2</sub> H <sub>5</sub> )C(O <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CH <sub>12</sub> =C(CH <sub>2</sub> H <sub>2</sub> C(C <sub>2</sub> H <sub>1</sub> ))(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>4</sub> H <sub>3</sub> C(C <sub>4</sub> H <sub>1</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>4</sub> H <sub>3</sub> SCH <sub>2</sub> C(C <sub>6</sub> H <sub>1</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C <sub>6</sub> H <sub>13</sub> C(C <sub>6</sub> H <sub>1</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> N-C <sub>6</sub> H <sub>13</sub> C(C <sub>6</sub> H <sub>1</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> None	n-C,H <sub>15</sub> C(C,H <sub>11</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> O) <sub>2</sub> C(C,H <sub>11</sub> )C(C,H <sub>11</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> n-C,H <sub>17</sub> C(C,H <sub>11</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>
$i \cdot C_3H_1BF$ $CH_2 = CHCH_2BF$ $HC = CCH_2BF$ $CH_2 = CBFCH_2BF$ $C_4 - C_8$	n-C <sub>4</sub> H <sub>9</sub> Br i-C <sub>4</sub> H <sub>9</sub> Br (C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> OHCH <sub>3</sub> Br 1,2-Dibromocydohexane	$\begin{array}{ll} \operatorname{Cit}_{C_0^1H_3^1\mathrm{CH} =} & \operatorname{Cit}_2 = \operatorname{CHCH}_2\mathrm{Br} \\ \operatorname{CHCH}(\mathrm{CH}_3) & C_1 - C_7 \end{array}$	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH(C <sub>2</sub> H <sub>5</sub> ) CH <sub>3</sub> I C <sub>2</sub> H <sub>5</sub> I C <sub>4</sub> H <sub>5</sub> CH <sub>2</sub> CI C <sub>4</sub> H <sub>5</sub> CH <sub>2</sub> CI C <sub>4</sub> L <sub>6</sub> O <sub>5</sub> CCCH <sub>5</sub> ). CH 7		$\begin{array}{cccc} & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & & \\ $		$\begin{array}{l} C_{1} A_{115DT} \\ (CH_{2})_{2} C(CH_{2})_{2} CI \\ n \cdot C_{3} H_{17BT} \\ Note: \text{ References } 577-1080 \text{ are on pp. } 322-331. \\ \ddagger \text{ The halogen was not specified.} \end{array}$

TABLE III—Continued

Alkylation of Monoalkylmalonic Esters,  $R'\mathrm{CH}(\mathrm{CO_2R})_2$  (The diethyl ester was used unless otherwise indicated.)

Refer- ence	906, 888 902	920 135 684 210	646 551 210	35 35 555	897	687 688, 687 555	282	687
Solvent	Toluene Ethanol	Ethanol Ethanol Ethanol Ethanol	Ethanol Ethanol Ethanol	6-С <sub>4</sub> П <sub>9</sub> ОН 6-С <sub>4</sub> П <sub>9</sub> ОП С <sub>6</sub> Н <sub>6</sub>	None	Ethanol C <sub>6</sub> H <sub>6</sub>	Ethanol	ı
Base	Na NaOC <sub>2</sub> H <sub>5</sub>	$NaOC_2H_5$ $NaOC_2H_6$ $NaOC_2H_5$ $NaOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>4</sub> H9-t NaOC <sub>4</sub> H9-t Na	Na	NaOC <sub>2</sub> H <sub>5</sub> Na	$NaOC_2H_5$	1
Yleld, %	2	8   4   45   45	78	62 76 85	I	777	ea. 70	I
Product	n-C <sub>10</sub> H <sub>21</sub> C(C <sub>6</sub> H <sub>13</sub> -n)(CO <sub>5</sub> C <sub>2</sub> H <sub>4</sub> ) <sub>2</sub> Diethyl $n$ -hexyl-( $d$ -eyelolæxylbutyl)-	malonate Dielityl n-hexyl-(n-undecenyl)malonate n-C, <sub>1</sub> H <sub>3</sub> 2(C <sub>6</sub> H <sub>13</sub> -n)(CO <sub>5</sub> C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> n-C, <sub>1</sub> H <sub>3</sub> C(C <sub>6</sub> H <sub>13</sub> -n)(CO <sub>5</sub> C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> Dielityl 2-methyleyclohexane-1,1-	$\begin{array}{l} \operatorname{tch}_{1}(\mathcal{C}_{2}H_{2}) \\ \operatorname{tch}_{2}(\mathcal{C}(\mathcal{H}_{2}) \mathcal{L}_{3}(\mathcal{C}(\mathcal{C}_{2}H_{2})) \\ \operatorname{tch}_{3}(\mathcal{C}(\mathcal{C}(\mathcal{H}_{3})\mathcal{C}(\mathcal{C}_{1}H_{2})\mathcal{C}) = \operatorname{CH}_{3}(\mathcal{C}(\mathcal{C}_{2}H_{2})) \\ \operatorname{Diethyl}_{3}(\mathcal{C}(\mathcal{H}_{3})\mathcal{C}(\mathcal{C}_{1}H_{3})\mathcal{C}) \\ \operatorname{Diethyl}_{3}(\mathcal{C}_{3}H_{3}) \\ \operatorname{CH}_{3}(\mathcal{C}_{3}H_{3}) \\ \operatorname{CH}_{3}(\mathcal{C}_{3}H_$	arearboxyrace Diethyl methyl-(3-hexyl)malonate Diethyl ethyl-(3-hexyl)malonate CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH(CH <sub>2</sub> )C <sub>3</sub> H <sub>2</sub> -n]CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	$\begin{matrix} 0 & \downarrow \\ -C_4 H_9 CH(CH_3) C(CH_2 C_4 H_3 S) (CO_2 C_2 H_5)_2 \end{matrix}$	(C2H5)2CHCH2C(CH3)(CO2C2H5)2 (C2H5)2CHCH2C(C2H5)(CO2C2H5)2 CH2CH2CH(C2H5)2CO2C2H5	OCO CH2CH2CICH2CH(C2H5)2JCO2C2H5	0
Alkylating Agent	C <sub>10</sub> -C <sub>18</sub> n-C <sub>10</sub> H <sub>21</sub> I 6-Cyelohexylbutyl bromide	n-Undecenyl bromide n-C <sub>16</sub> H33I n-C <sub>18</sub> H37I None	$C_2H_3O(CH_2)_4Br$ $CH_2=CHCH_2Br$ None	$\operatorname{CH}_3\mathbf{X}_{\sharp}^*$ $\operatorname{C}_2\mathbf{H}_3\mathbf{X}_{\sharp}^*$ $\operatorname{Br}(\operatorname{CH}_2)_2\operatorname{Br}$	2-Chloromethylthlophene	$C_1$ – $C_3$ CH <sub>3</sub> Br $C_2$ H <sub>6</sub> Br Br(CH <sub>2</sub> ) <sub>2</sub> Br	CH2—CH2	°o′ n-C <sub>3</sub> H <sub>7</sub> Br
R,	n-C <sub>d</sub> U <sub>13</sub> (Cont.)	CU3CHBr(CH2)4	C2H5O(CH5)4 n·C3H,CH(CH5) Br(CH2)4CH(CH5)	3-Hexyl n-C <sub>3</sub> H <sub>7</sub> CH(CH <sub>3</sub> )CH <sub>2</sub>	i.C,HoCH(CH3)	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CII CII <sub>2</sub>		

÷.					
$C_{11}$ SCH <sub>2</sub> CI $C_{211}$ SCH <sub>2</sub> CI $C_{11}$ SCH <sub>2</sub> CI $C_{11}$ = CHCH <sub>2</sub> I	$\begin{array}{l} C_2 \Pi_4 \mathrm{SCH}_2 \mathrm{CC}_2 \Pi_5 \mathrm{NCO}_2 \mathrm{C}_2 \Pi_6 \mathrm{J}_2 \\ C_2 \Pi_5 \mathrm{CCH}_2 \mathrm{CC}_2 \Pi_5 \mathrm{J} (\mathrm{CO}_2 \mathrm{C}_2 \Pi_6 \mathrm{J}_3 \\ \mathrm{CH}_3 = \mathrm{CH} \mathrm{CH}_2 \mathrm{CC}_2 \mathrm{H}_5 \mathrm{NCO}_2 \mathrm{C}_2 \Pi_6 \mathrm{J}_2 \end{array}$	84	Na NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ether Tolucne Ethanol	205 125 79
Cl(Cl1 <sub>2</sub> ) <sub>2</sub> CN Br(Cl1 <sub>2</sub> ) <sub>3</sub> Br I(Cl1 <sub>2</sub> ) <sub>3</sub> I	NC(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>4</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Br(CH <sub>2</sub> ) <sub>3</sub> C(C <sub>4</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> None	; [ ]	$NaOC_2H_5$ $Na$ $NaOC_2H_5$	Ethanol None Ethanol	932 120 02
$C_4$ $n$ - $C_4$ $ll_3$ $ll_7$ $CI1_2 = CI10(CI1_2)_2$ $CI$ $C_2$ $ll_3$ $S(CI1_2)_3$ $CI$	$n \cdot C_4 \Pi_0 C(C_6 \Pi_b) (CO_3 C_2 \Pi_s)_2$ $C\Pi_2 = C\Pi O(C\Pi_2)_2 C(C_6 \Pi_b) (CO_2 C_2 \Pi_b)_2$ $C_2 \Pi_5 S(C\Pi_2)_2 C(C_6 \Pi_b) (CO_2 C_2 \Pi_5)_2$	68 62 70-90	NaOC <u>2</u> II5 Na NaOC <sub>2</sub> II6	Ethanol Ether Toluene	142 331 553
1(CII <sub>2</sub> ) <sub>3</sub> CN C <sub>5</sub> -C <sub>6</sub>	NC(CH2)3C(C4H5)(CO2C2H5)2	٧ 43	Na	Toluene	3
2-Chloromethyltilepheno 2-Chlorotetralydropyran	Dicthyl phenyl-(2-thenyl)malonate Dicthyl phenyl-(2-tetrahydropyranyl)	1-1	NaOC2Us NaH	Ethanol Toluene	50 683
Br(CH <sub>2</sub> ) <sub>d</sub> Br	malonato (C <sub>2</sub> 11 <sub>5</sub> 0 <sub>2</sub> C) <sub>2</sub> C(C11 <sub>2</sub> ) <sub>0</sub> C(CO <sub>2</sub> C <sub>2</sub> Π <sub>5</sub> ) <sub>2</sub>	ı	Na	Xyleno	670
2 Cyclohexenyl bromlde	Colls Colls Diefliel nhenvi-(2-evolohevenvilmalonale	12	TOCH	ر تا	634
1,2 Dibromocyclohexane	District Income (2-cyclohexenyl)malonato	323	NaOC <sub>2</sub> II <sub>6</sub>	Ethanol	911, 933
Conscitation Consc	C4115C112C(C4115)(CO2C2115)2 C4115C11(C113)C(C4115)(CO2C3115)3	3	NaUC <sub>2</sub> II <sub>5</sub>	Ethanol	182 934
CallsO(CII2)2CI	Cq1150(C112)2C(CqH5)(CO2C2115)2	Ţ	I	1	374
$C_9$ - $C_{16}$					
I(CII,),CII(C2,II,5)1 I(CII,1),CII(CO,C,II,1),	CellsCH(Cells)C(Cells)(CO <sub>2</sub> C <sub>2</sub> H <sub>6</sub> ); (CellsO <sub>2</sub> C),CH(CH <sub>2</sub> ),C(C <sub>2</sub> H <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> );	1 5	ا ا	Tolyone	934
p-t.C,IIoCoII,(CII2)2Br	p.t. C411, C&II 4(CII2), C(CQII5)(CO2C2II5)2	40	Na	Toluene	321
1(CH2)10CO2C2H3	C2II,6O2C(C112)10C(C6II,6)(CO2C2II,6)2	[	Na	Toluene	35
P-Cyclonexylphenyl)ethyl bromldo	Dictiyl phenyi-{\(\beta\coperation p \) cfivilmalonate	44	Na	Xylene	935
ո. Այց Սյոյ հե	n-C161131C(C6IIs)(CO2C2IIs)2	452	Na	Xylene	679
rences 577-1080 are on pp. 322-331.					

# TABLE III-Continued

Alkylation of Monoakkylationic Esters, R'CH(CO<sub>2</sub>R)<sub>2</sub>

diethyl ester was used unless otherwise indicated.)

									C	R	.G	AN	VIC.	R	EA	C'.	rions												
	Refer-	спео	929		100	T 0	21 0	930	35	8	125		215	287			169 182	51	51 44	227	375	331, 571	51, 44	330, 800	931	92	92	787	
		Solvent	Ethanol		Xylene	Ethanoi	Ethanol	Tolucne	Ethanol	Ethanol	Polucue		Ethanol	None			Ethanol Ethanol	(C21150)2C0	Ethanol	(031180)300	спрои	Ethanol	(C <sub>2</sub> H <sub>6</sub> O) <sub>2</sub> CO	022(05H2)	Toluene	Ethanol	Ethanol	Ethanol	
(17.700)		13,080	NaOCalfa	1	Na	NnOC2II	NnOC.H.	N	NAOC.H.	No OC. II.	No OC. II.	744002445	$NnOC_2H_5$	N T	4		$ m NaOC_2H_6$ $ m NaOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> 115	NaOCH	NaOC,IIs	$Mg(OC_2\Pi_5)_2$	NaOC <sub>2</sub> II <sub>5</sub>	NaII	NaOC <sub>2</sub> H <sub>5</sub>	$NaOC_2H_5$	$NaOC_2II_5$	
20 111011	No.	11cld	: 1	l	45	ļ	į	ļ	. 1	ì	i	i	40	1 2	ŝ		09     06	81	0.2	8	92	15	•00	30	59	0	50	ca. 70	
(The diethyl ester was used unless otherwise markets)	•	1	Lroduct	Diethyl cyclohexyl-(\$\text{\$\theta\$-cyclohexylethyl}).	minoning management of the control o	Control of the Contro	7-CalligC(Callift) 7.2.16/2	n-C10H31C(C6H11)(CC2C2H5/2	Dicthyl cyclohexyl(gernnyl)inglonnic	n-C11[[23C(C6[[11])(CO2C2[[6])2	$n$ - $C_{12}H_{23}C(C_6H_{11})(CO_2C_2H_5)_3$	C211,8C11,C(C411,)(CO2,C211,5)2	$G(r) = C(G(r), G(G, II_k)(GO, G, II_k),$	C, II2SCII2C(C, II6)(CO, C, II6);	Diethyl hydnocarpyl-(2-cyclolicxenyl)- malonate		$\begin{array}{l} C_6\Pi_6C(C\Pi_2)(CO_2C_2\Pi_5)_2 \\ C_6\Pi_5C(C\Pi_2)(CO_2C_2\Pi_5)_2 \end{array}$	C, II, C(C, II,)(CO, C, II,),	Can c(cans)(coacans)	$C_6H_5C(C_2H_6)(CO_2C_2H_5)_2$	O II OW II WOO OH Y.	CHISCO2013/2	2,H.;Q(Q;H;)(QQ,H;);	C.H.C.C.H.J.CO.C.H.J.	Br(CH,),C(C,H,)(CO,C,H,),	None	(C, H, O, C), C(C, H, ) C(C, H, ) (CO, C, H, ),	CH2CH2C(C,H5)CO2C2H5	020
(Трө с		Alkylating	Agent	p.Cyclohexylethyl bromida		21-Cp 11 1915r	n.C,111,13r	n-C,0ff2, Br	Geranyl chloride	".C. II. Br	n.CflasBr	C. II. SCIII.CI		Cluster Cite Custor 2. Chloromethylthlophene	Hydnocarpyl bromide-KI	ζ.	$c_1$ $c_{11}$ $c_{11}$	5 5	C.H.Br	C <sub>2</sub> H <sub>5</sub> Br	,		C21151		nroll 1. In	n-(CII.).Br	1/011.7	CIL CIL	0
			11,	Cyclohexyl(~Call11)	(Cont.)							1.Cyclohexenvl	(=C,U,)		2.Cyclohexenyl		Phenyl												

#### THE ALKYLATION OF ESTERS AND NITRILES

						-
205 125 79 932 129 92	142 331 553 92	50 683	629	534 911, 933 182 934 374	934 92 321 92	629
Ether Toluene Ethanol Ethanol None Ethanol	Ethanol Ether Toluene Toluene	Ethanol Toluene	Xyleno	C <sub>6</sub> H <sub>6</sub> Ethanol Ethanol	Tolueno Toluene Toluene Xylene	Xylene -
Na NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> Na	NaOC <sub>2</sub> H <sub>5</sub> Na NaOC <sub>2</sub> H <sub>5</sub> Na	NaOC <u>.</u> H <sub>s</sub> NaH	Na	KOCH, NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Na Na Na Na	Na
8     8	58 52 70-90 > 43	11	1	55 55	169 1 #	er <del>T</del>
$C_2H_5 S C H_2 (C_6H_5) (CO_2C_2H_5)_2$ $C_2H_5 S C H_2 (C_6H_5) (CO_2C_2H_3)_2$ $C H_3 = C H C H_2 (C_6H_5) (CO_2C_2H_5)_2$ $N C (CH_2)_2 C C_6H_3) (CO_2C_2H_5)_2$ $Br (CH_2)_2 C C_6H_3) (CO_2C_2H_5)_2$ $None$	$\begin{array}{l} n\cdot C_4 H_0 C(C_6 H_5) (CO_2 C_2 H_5)_2 \\ CH_2 = CHO(CH_2)_2 C(C_6 H_5) (CO_2 C_2 H_5)_2 \\ C_2 H_5 S(CH_2)_2 C(C_6 H_5) (CO_2 C_2 H_5)_2 \\ NC(CH_2)_3 C(C_6 H_6) (CO_2 C_2 H_5)_2 \end{array}$	Diethyl phenyl-(2-thenyl)malonato Diethyl phenyl-(2-tetrallydropyranyl) malonate	$(c_2H_5O_2C)_2C(CH_2)_6C(CO_2C_2H_5)_2$	GeHs, CeHs Diethyl phenyl-(2-cyclohexenyl)malonate Diethyl phenyl-(2-cyclohexenyl)malonate GeHsGHGGG,HSGCO <sub>2</sub> CeHs,2 CeHsGHGCH <sub>2</sub> O(CeHs)(CO <sub>2</sub> CeHs)2 CeHsO(CH <sub>2</sub> )2(CeHs)(CO <sub>2</sub> CeHs)2	C <sub>6</sub> H <sub>5</sub> CH(C <sub>2</sub> H <sub>5</sub> )C(C <sub>6</sub> H <sub>5</sub> )(CO <sub>3</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CH(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> p-t-C <sub>1</sub> H <sub>3</sub> C <sub>6</sub> H <sub>4</sub> (CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>2</sub> H <sub>5</sub> O <sub>3</sub> C(CH <sub>3</sub> ) <sub>10</sub> C(C <sub>6</sub> H <sub>5</sub> )(CO <sub>3</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Diethyi phenyi-fe-(p-cyclohexyiphenyi)	//-''14 <sup>11</sup> 33 <sup>(</sup> (C <sub>4</sub> 115)(CO <sub>3</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>
$C_2H_5 SCH_2 CI$ $C_2H_5 SCH_2 CI$ $CI_2 = CICCH_2 I$ $CI(CH_2)_2 CN$ $CI(CH_2)_2 CN$ $CI(CH_2)_3 Br$ $I(CH_2)_3 I$	$n$ - $C_4H_9Br$ $CH_2 = CHO(CH_2)_2CI$ $C_2H_5S(CH_2)_2CI$ $I(CH_2)_2CN$ $C_5-C_6$	2-Chloromethythlophene 2-Chlorotetrahydropyran BrCHAAR	10.80	2 Cyclohexenyl bromide 1.2 Dibromocyclohexano $G_6H_5\mathrm{CH}_2\mathrm{Cl}$ $G_6H_5\mathrm{CH}(\mathrm{CH}_3)\mathrm{I}$ $G_6H_5\mathrm{Cl}(\mathrm{CH}_3)\mathrm{I}$ $G_6H_5\mathrm{Cl}(\mathrm{CH}_3)\mathrm{I}$ $G_9-G_{16}$	$C_6\Pi_5\mathrm{CH}(C_2\Pi_6)\mathrm{I}$ $I(G\Pi_2)_3\mathrm{CH}(GO_3,C_2\Pi_3)_2$ $P^{**}(C_4\Pi_3)_4\mathrm{CH}_4(G\Pi_2)_3\mathrm{Br}$ $I(G\Pi_2)_4\mathrm{CO}_3,C_3\Pi_3$ $P^{**}(P^*Cyclohewylphenylphe$	rences 577-1080 are on pp. 822-831. A ceter was used in this experiment, nts were added in Inverse enter.

920 135 201 718, 748 718 897 720	206 663	32	32 32 32 50, 709	8 8 8 8 8 8 8 8	147	937	938 144, 615	930
Ethanol Ethanol Toluene Ethanol None Ethanol	Etlianol (C <sub>2</sub> H <sub>s</sub> O) <sub>2</sub> CO	Ethanol	Ethanol Ethanol Ethanol Ethanol	Ethanol Ethanol Ethanol Ethanol	Tolucne Toluene	Ethanol	C <sub>6</sub> H <sub>6</sub> Ethanol	
NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> K NaOC <sub>2</sub> H <sub>5</sub> Na NaOC <sub>2</sub> H <sub>5</sub> Na	$ m NaOC_2H_5 \ NaOC_2H_5$	NaOC <sub>2</sub> H <sub>s</sub>	NaOC2H5 NaOC2H5 NaOC2H5 NaOC2H5	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>3</sub> H <sub>5</sub> NaOC <sub>3</sub> H <sub>5</sub>	N N N	Na0C <sub>2</sub> H <sub>6</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	
1832818	18	ì	1111	1111	8 1	09	80 63	
Dictityl n-heptyl-(n-undecenyl)malonate $n$ -C <sub>1</sub> aH <sub>3</sub> 2(Cr <sub>1</sub> H <sub>13</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> Dicthyl n-heptyl-(hydnocarpyl)malonate $i$ -C, $\Pi$ <sub>1</sub> s(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> $i$ -C, $\Pi$ <sub>1</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> $i$ -C, $\Pi$ <sub>1</sub> C(CH <sub>3</sub> )(CCH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> $n$ -C, $\Pi$ <sub>0</sub> C(CH <sub>2</sub> )(CCH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> $C_{2}$ H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> CH(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	$C_8H_5O(CH_2)_2 _C(CO_2C_2H_5)_2$ Diethyl ethyl· $[\beta$ -(eyelopentylldene)ethyl]- malonatø	C2H6C(C7H13XCO2C2H5)2	n-C <sub>3</sub> H-C(C,H <sub>13</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ), n-C <sub>4</sub> H <sub>9</sub> C(C,H <sub>13</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ), n-C <sub>5</sub> H <sub>11</sub> C(C,H <sub>13</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ), Dietityl (codolosylmethyl)-2.	n-C <sub>2</sub> H <sub>13</sub> C(C <sub>2</sub> H <sub>13</sub> ) n-C <sub>2</sub> H <sub>13</sub> C(C <sub>2</sub> H <sub>13</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>13</sub> ) n-C <sub>2</sub> H <sub>17</sub> C(C <sub>2</sub> H <sub>13</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>13</sub> ) Diethyl (eyelohexylmethyl)-	(\$-cyclohexylethyl)malonate Dicthyl di-(2-methylcyclohexyl)malonate Diethyl gcranyl-(2-methylcyclohexyl).	matonate $C_2H_5O_2CC(CH_3) = C(CH_3)C(CH_3)(CO_2C_2H_5)_2$	$c_{_{\boldsymbol{d}}\boldsymbol{H}_{\boldsymbol{b}}}CH_{_{\boldsymbol{a}}}C(CH_{_{\boldsymbol{a}}})(CO_{_{\boldsymbol{a}}}C_{_{\boldsymbol{d}}\boldsymbol{H}_{\boldsymbol{b}}})_{\boldsymbol{a}}\\ c_{_{\boldsymbol{d}}}H_{_{\boldsymbol{a}}}CH_{_{\boldsymbol{a}}}C(CH_{_{\boldsymbol{a}}})(CO_{_{\boldsymbol{a}}}C_{_{\boldsymbol{a}}}H_{_{\boldsymbol{b}}})_{\boldsymbol{a}}\\$	
n-Undecenyl bromlde n-C <sub>10</sub> H <sub>33</sub> L Ifydnocarpyl chloride CH <sub>3</sub> I CG <sub>3</sub> I 2-Chloromethyllilopheno i <sub>3</sub> ) n-C <sub>5</sub> H <sub>11</sub> Br	C <sub>6</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>2</sub> Br Not stated CC.	$c_2H_5Br$	n-C <sub>2</sub> H,Br n-C <sub>4</sub> H <sub>3</sub> Br n-C <sub>5</sub> H <sub>11</sub> Br 2-Chtoromethyltiliopheno	n-C <sub>0</sub> H <sub>13</sub> Br n-C <sub>1</sub> H <sub>15</sub> Br n-C <sub>5</sub> H <sub>17</sub> Br β-Cyclohexylethyl bromide	2-Methylcydohexyl bromlde Gcranyl chloride	$_{\tilde{a}}^{\mathrm{CH}_{3}\mathrm{I}}$	С <sub>Г</sub> СН <sub>3</sub> I СН <sub>3</sub> I	Note: References 577-1080 are on pp. 322-331.
n-Undecen: n-C <sub>16</sub> H <sub>33</sub> I Hydnocarp c-C <sub>2</sub> H <sub>15</sub> i-C <sub>2</sub> H <sub>1</sub> CH(CH <sub>3</sub> ) n-C <sub>4</sub> H <sub>6</sub> CH(C <sub>2</sub> H <sub>5</sub> ) C-C <sub>3</sub> H c-C <sub>4</sub> H <sub>6</sub> CH(C <sub>4</sub> H <sub>5</sub> ) C-C <sub>4</sub> H <sub>6</sub> O <sub>4</sub> C(CH <sub>2</sub> ), 2CH(CH <sub>3</sub> ) n-C <sub>5</sub> H <sub>1</sub> Dr	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> β-Cyclopentylidenc- cthyl	Cyclohexylmcthyl	(		2-Mcthylcyclohexyl	$C_2H_5O_2CC(CH_3) = C(CH_3)$	$\mathrm{c_{_6}H_5\mathrm{CH}_2}$	Note: References

True. Activities 577-1080 are on pp. 322-331 The halogen was not specified.

TABLE III-Continued

R'CII(CO,R)2	indicated.)
Esters,	Herwise
ALEVIATION OF MONOALKYLMALONIC ESTERS, R'CH(CO.R).	orth diethyl ogter was used unless otherwise indicated.)
ALKYLATION OF A	ter free died by

AIRy fating	Preduct	Yield,	Виче	Solvent	Refer-
Skeni Clich	(C,11,0,10),C(C11,0C11C(C0,C,115))	ı	Na	ı	121
	çırşCetr <sub>s</sub>				
C. 11, 21C	*(*11 <sup>5</sup> 2 <sup>6</sup> 02)(*11 <sup>5</sup> 0)2 <sup>5</sup> 112 <sup>8</sup> 11,	80	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	121, 141
entachter entschter ment enne	(TI,0CH,C(CH,G,U,X)CO₁C₁U,3; CH,SCH,C(CH,G,U,X)CO₂C₁U,3; n:CH-CCH(CH,G,U,XCO₁C₁U,3; CH,C(CH,C,U,3O0,C2H,3	78 71 7 60.70	Na NaOC <sub>2</sub> II,-i K NaOC <sub>2</sub> II <sub>5</sub>	Ether i-C <sub>3</sub> 11,01f Ether Ethanol	910 205 911
	030				
C,3 C,11,8CH,Cl i-C,11,11r Cl(CH,2)31r	c,tr,scu,gcm,g,u,yco,c,u, ic,ti,ccn,c,ii,yco,c,ii,s, ic,ii,o,c,ic,ic,ii,loo,c,ii,s,	1 23	$Na$ $NaOC_2II_5$ $NaOC_2II_5$	Ether Ethanol Ethanol	205 144 530
į	CIT2C6IT5				
C't n-C <sub>4</sub> [1] <sub>3</sub> Br	1.C. 11.0C(C11.0C.11.5)(CO.2.0.11.5).	65	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	144
n-C <sub>1</sub> Π <sub>p</sub> Γ (n-C <sub>1</sub> Π <sub>p</sub> Ο) <sub>2</sub> CO	n-C,11,C(C1f2C <sub>6</sub> F13)(CO <sub>2</sub> C <sub>2</sub> H3) <sub>2</sub> n-C,11 <sub>9</sub> C(C1f <sub>2</sub> C <sub>6</sub> H3)(CO <sub>2</sub> C <sub>1</sub> H <sub>9</sub> -n) <sub>2</sub> ¶	80	KOC <sub>4</sub> II <sub>9</sub> ·n	(n-C,H <sub>9</sub> O) <sub>2</sub> CO	330, 890
:-C <sub>1</sub> [1], Br C C 1, CO <sub>2</sub> C <sub>2</sub> 11, C 1, CC  == C 1 C 1, C	$i\cdot c_1 \Pi_s C(G\Pi_s C_s \Pi_s) GO_s C_s \Pi_s)_s$ $C_s \Pi_s O_s CG\Pi_s C(G\Pi_s C_s \Pi_s) CO_s C_s \Pi_s)_s$ $G\Pi_s CG := G\Pi G\Pi_s C(G\Pi_s C_s \Pi_s) CO_s C_s \Pi_s)_s$	42 00	NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub> NaOC <sub>2</sub> II <sub>5</sub>	Ethanol Ethanol Ethanol	144 108 916
C <sub>5</sub> -C <sub>7</sub> n-C <sub>3</sub> H <sub>11</sub> X; i-C <sub>3</sub> H <sub>11</sub> Br Cl(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> G <sub>3</sub> H <sub>3</sub>	n-C,11,1C(C(1,C,14,)(CO,C,14,); i-C,11,1C(C(1,2,4,1,)(CO,C,14,); C,11,0,C(C(1,2,0,1,1)(CO,C,14,);	35	NaOC <sub>2</sub> U <sub>5</sub>	Ethanol None	942 144 830
	Mk) ratins  Agent  Cilici  C <sub>1</sub> Cilici  Cili	רי. וו, וו, וו, ריי	Preduct (C <sub>1</sub> II <sub>2</sub> O <sub>2</sub> C) <sub>2</sub> C(C'II <sub>2</sub> C <sub>4</sub> II <sub>2</sub> )C'IICIC(CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )    C <sub>1</sub> I <sub>3</sub> C <sub>1</sub> C <sub>4</sub> C <sub>4</sub> II <sub>2</sub> )CC <sub>2</sub> C <sub>3</sub> II <sub>3</sub> )   C'I <sub>3</sub> CCII <sub>3</sub> C(C <sub>1</sub> I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C'I <sub>3</sub> CCII <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C'I <sub>3</sub> CCII <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C'I <sub>4</sub> CCII <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CC <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CC <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CC <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> II <sub>3</sub> )CO <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )CC <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )CC <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )CC <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )CC <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>1</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )CC <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> C(C <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )C(C <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )C(C <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )C(C <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )C(C <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )C(C <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )C(C <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )C(C <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )C(C <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )C(C <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )C(C <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )C(C <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )C(C <sub>2</sub> C <sub>4</sub> II <sub>3</sub> )   C' <sub>4</sub> I <sub>4</sub> I <sub>4</sub> C(C'I <sub>4</sub> C <sub>4</sub> I <sub>4</sub> )C(C <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )C(C <sub>4</sub> I <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )C(C <sub>4</sub> C <sub>4</sub> I <sub>3</sub> )C	Yreduct   C <sub>1</sub> (1 <sub>1</sub> , O <sub>2</sub> C) <sub>2</sub> ((C)(1 <sub>1</sub> , C, HC)(C)(C, H <sub>2</sub> ) <sub>2</sub>   C   C <sub>1</sub> (1 <sub>2</sub> , O <sub>2</sub> C)(C)(C)(C, H <sub>2</sub> ) <sub>2</sub>   C   C   C <sub>1</sub> (1 <sub>2</sub> , O <sub>2</sub> C)(C)(C, H <sub>2</sub> )   C   C   C <sub>2</sub> (1 <sub>1</sub> , O <sub>2</sub> C)(C)(C)(C, H <sub>2</sub> )   C   C   C   C   C   C   C   C   C	Product   Signature   Signa

TABLE III—Continued

THON OF MONOALKYLMALONIC ESTERS,  $R'CH(CO_2R)_2$ 

Rofor.	ence	890, 330 282	743 947	897 725	928	906,888 31,902	135	746 746 545	746	746 897 746
	Solvent	(C <sub>2</sub> II <sub>5</sub> O) <sub>2</sub> CO Ethanol	Ethanol	None Ethanol	Ethanol	Toluene Xylene	Ethanol	Ethanol	1	None
ted.)	Ваяс	$NaOC_2H_5$ $NaOC_2H_5$	NaOC <sub>2</sub> II <sub>5</sub>	Na NaOC <sub>2</sub> II <sub>S</sub>	NaOC <sub>2</sub> H <sub>5</sub>	Na Na	NaOC <sub>2</sub> H <sub>5</sub>	Na OC <sub>2</sub> H <sub>5</sub>	1	Na l
, so indice	Yleld, %	33 (50)§ ca. 70	1 1	20-60	1	60 52	84	96 85 70-85	9	60
ALKYLATION OF MONOALKY LAMADONA AND ALKYLATION OF MONOALKY LAMADONA (The diethyl ester was used unless otherwise indicated.)	Product	$n$ - $C_8$ II $_{17}$ C( $C_2$ II $_5$ )(CO $_2$ C $_2$ II $_5$ ) $_2$ CH $_2$ CH $_2$ C( $C_8$ II $_{17}$ *1)CO $_2$ C $_2$ II $_5$	$\begin{array}{c c} 0 & -CO \\ \hline CII_3 = CHCH_2(CC_8\Pi_{17^{-10}})(CO_2C_2\Pi_5)_2 \\ \hline CII_3 = CHCH_2(CC_8\Pi_{17^{-10}})(CO_2C_2\Pi_5)_2 \\ \hline CII_3 = CHCH_2(CC_8\Pi_{17^{-10}})(CO_2C_2\Pi_5)_2 \\ \hline CII_4 = CHCH_2(CC_8\Pi_{17^{-10}})(CO_2C_2\Pi_5)_2 \\ \hline CII_5 = CHCH_2(CC_8\Pi_5)(CO_2C_5\Pi_5)_2 \\ \hline CII_5 = CHCH_2(CC_8\Pi_5)(CC_8\Pi_5)_2 \\ \hline CII_5 = CHCH$	Diethy arcocy, $CC_{2,C}$ $C_{2,C}$ $C_{2,C}$ $C_{2,C}$ $C_{1,C}$ $C_{2,C}$ $C_{1,C}$ $C_{2,C}$ $C_{1,C}$ $C_{2,C}$ $C_{1,C}$ $C_{2,C}$	Dienistrate (1997) - 1997 - 19	Digthy mocey-th/ $\langle z   z \rangle$ and ethyllmalonate ( $n$ - $C_8H_{1/2}$ 2C( $C_0Z_2H_0$ ).	Denote the following $n$ -C <sub>16</sub> H <sub>33</sub> C(C <sub>8</sub> H <sub>17</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	$n\cdot C_0\Pi_{13}\mathrm{CH}(\mathrm{CH_3})\mathrm{C}(\mathrm{CH_3})(\mathrm{CO_2}C_2\Pi_5)_2 \\ n\cdot C_6\Pi_{13}\mathrm{CH}(\mathrm{CH_3})\mathrm{C}(C_3\Pi_5)^2 + n)(\mathrm{CO_2}C_2\Pi_5)_2 \\ n\cdot C_6\Pi_{13}\mathrm{CH}(\mathrm{CH_3})\mathrm{C}(\mathrm{CO_2}C_2\Pi_5)_2$	$\overset{CH_{2}}{n \cdot C_{0} \Pi_{13} CH (CH_{3})} \overset{CH_{2} CII = CH_{2}}{CI(CH_{3})} C(CO_{2} C_{2} \Pi_{5})_{2}$	$\begin{array}{l} \mathrm{i}_{1}\mathrm{C}_{1}\mathrm{C}_{1}\mathrm{C}_{2}\mathrm{I}_{5} \\ n.\mathrm{C}_{6}\mathrm{H}_{13}\mathrm{CH}(\mathrm{CH}_{3})\mathrm{C}_{5}\mathrm{H}_{11}\mathrm{^{-3}}\mathrm{N}(\mathrm{Co}_{2}\mathrm{C}_{3}\mathrm{H}_{3})_{2} \\ n.\mathrm{C}_{6}\mathrm{H}_{13}\mathrm{CH}(\mathrm{CH}_{3})\mathrm{C}_{6}\mathrm{H}_{15}\mathrm{^{-3}}\mathrm{H}_{3}\mathrm{SN}(\mathrm{Co}_{2}\mathrm{C}_{2}\mathrm{H}_{5})_{2} \\ n.\mathrm{C}_{6}\mathrm{H}_{13}\mathrm{CH}(\mathrm{CH}_{3})\mathrm{C}_{6}\mathrm{H}_{15}\mathrm{^{-3}}\mathrm{N}\mathrm{N}\mathrm{Co}_{2}\mathrm{C}_{2}\mathrm{H}_{5})_{2} \end{array}$
ALKYLAT: (The d	Alkylatiog	$C_2 - C_{1d}$ (C <sub>2</sub> II <sub>5</sub> O) <sub>2</sub> CO (C <sub>1</sub> II <sub>2</sub> O) <sub>2</sub> CO	CH <sub>2</sub> =CHCH <sub>2</sub> Br	Cyclobutylmethyl bromide 2-Chloromethylthlophene	g.Cyclopentylethyl bromiae	β-(2-Cyclopentenyl)cthyl bromide n-C <sub>8</sub> H <sub>17</sub> I	$ ho$ -Cyclohexylcthyl bromuc $n$ - $C_{16}\Pi_{33}^{ m I}$	$C_1$ - $C_7$ $CH_3$ $Br$ $r$ - $C_3$ $H_7$ $Br$ $CH_2$ = $CHCH_2$ $Br$	$_{\mathrm{G_2H_6CH(CH_3)CH_2Br}}$	$i$ - $C_{\rm s}H_{11}{ m Br}$ 2-Chloromethylthiophene $n$ - $C_{ m r}H_{16}{ m Br}$
		$\Gamma_{\mathcal{S}}$ $G_{\mathcal{S}}$ $n$ – $C_{\mathcal{S}}\Pi_{17}$						$n$ - $\mathrm{C}_{\mathrm{d}}\mathrm{H}_{13}\mathrm{CH}(\mathrm{CH}_{3})$		

#### THE ALKYLATION OF ESTERS AND NITRIL

	65.5	c						RS AND	NITRILES	
	13	212	108	\$	38	8 8	45 to 15 to	374 755 755, 565	142 374 755 755 919	
	Xyles	Efficient	None	(C <sub>2</sub> H <sub>2</sub> O) <sub>2</sub> CO	(C <sub>2</sub> H <sub>2</sub> O) <sub>2</sub> CO	(۲ <sub>,</sub> ۱۱ <sub>,</sub> ۲۵) (۲ <sub>,</sub> ۱۱ <sub>,</sub> ۲۵)	Toluene Ethanol Ethanol	Ethanol Ethanol	Ethanol Ethanol Ethanol Cthanol	
			ž.			NaOC <sub>1</sub> H <sub>2</sub>	Ns NsOC <sub>3</sub> H <sub>3</sub> NsOC <sub>3</sub> H <sub>3</sub>	NaOC <sub>2</sub> II <sub>5</sub>	NaOC <sub>1</sub> II <sub>5</sub> NaOC <sub>1</sub> II <sub>5</sub> NaOC <sub>1</sub> II <sub>5</sub> K	the yiekt.
,	<u>.</u>	i	1	1 1	ි දි දි	8	22111	£ 5	11128	resents
i-C <sub>4</sub> 11 <sub>13</sub> CH(CH <sub>2</sub> )Ç(CO <sub>2</sub> C,H <sub>2</sub> ),	$(C\Pi_1)_1\Omega C_3\Pi_3$ $n$ $C_1\Pi_4C\Pi (C_1\Pi_3)C\Pi_2(C_1C_3C_3\Pi_3)$				malonate Dichyl ethylf2-cyclohevylldeneithyl). malonate	Dicthyl di (p. cyclohevylidencëdiyi). malonate	C <sub>6</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(C <sub>1</sub> H <sub>3</sub> )(CO <sub>1</sub> C <sub>1</sub> H <sub>2</sub> ) C <sub>6</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>2</sub> )(CO <sub>1</sub> C <sub>1</sub> H <sub>2</sub> ) C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> C <sub>1</sub> H <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> C <sub>1</sub> H <sub>3</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CO <sub>1</sub> C <sub>2</sub> H <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>3</sub> C <sub>1</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> )C(CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> )C(CH <sub>2</sub> )C(C	C <sub>4</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> ) <sub>3</sub> C(C <sub>2</sub> C <sub>1</sub> H <sub>3</sub> ) <sub>3</sub> C <sub>4</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> C(C <sub>1</sub> H <sub>2</sub> -n)(CO <sub>2</sub> C <sub>1</sub> H <sub>3</sub> ) <sub>3</sub> C <sub>4</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>3</sub> ) <sub>3</sub> C <sub>4</sub> H <sub>3</sub> (CO <sub>2</sub> C <sub>1</sub> H <sub>3</sub> ) <sub>3</sub>	Carson 1,14(C) II - (cc)(CO, C, II, 2) - (cd)(CO, C, II, 2) - (cd)(C) II - (cd)(C)	the figure represents the conversion; the figure in parentheses represents the yield.
C <sub>2</sub> II <sub>5</sub> O(CII <sub>2</sub> ) <sub>2</sub> I	$CII_2 = CIICII_2\Pi_F$	2-Chloromethylthlophene	2-Chloromethylthlophene	β-Cyclohexylethylbromkle CH <sub>2</sub> X‡	$c_{i}II_{s}X_{s}$	hallde $\ddagger$ $C_2$ $C_3$	C <sub>2</sub> H <sub>3</sub> Br n-C <sub>2</sub> H <sub>3</sub> Br n-C <sub>2</sub> H <sub>3</sub> Br i-C <sub>3</sub> H <sub>3</sub> Br i-C <sub>3</sub> H <sub>3</sub> Br i-C <sub>3</sub> H <sub>3</sub> Br	C4-C3 n-C1H <sub>0</sub> 1 c1H <sub>2</sub> O(CH <sub>2</sub> ),C1 sec-C <sub>1</sub> H <sub>2</sub> X;	CHISCO = CHCILICO CYGOROUP BY 1970 A 222-331.	and the first figure repr
$i \cdot C_b \Pi_{12} \text{CH}(\text{CH}_2)$	$^{n\text{-}C_4^{\text{II}_0}\text{CII}(C_4^{\text{II}_5})\text{CII}_2}$		\$-Cyclohexylethy1	\$-Cyclohexylideneethyl CifzX\$		$C_{\mathfrak{g}}H_{\mathfrak{s}}(\mathbb{C}\Pi_{\mathfrak{s}})_{\mathfrak{s}}$		,	CHAPTE CHAPTE CHAPTE CASOPORTY Dromide Note: References 577-1080 are on pp. 322-331, \$ Here and In subsequent, not specified.	

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		Solvent	Ethanol		ľ	Ethanol	Ethanol Ethanol	Ethanol	Tolucne	I	Ethanol	Ethanol Ethanol	1	Toluene	l	١	•	Toluene		l		
CO.R.	tod.)	Base	NaOC <sub>2</sub> U <sub>5</sub>	$NaOC_2\Pi_5$		NaOC <sub>2</sub> 11 <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> TI <sub>S</sub>	Na	1	NaOC, III	NaOC.115	NaOC <sub>2</sub> ns	$NaOC_2II_5$	Ī	1	l	NaOC <sub>2</sub> H <sub>5</sub>		١		
	r CLL	ield. %	75	01		1 %	<del>1</del> 9	1 1	62	1	1 8	5 9	8 6	2 82	. 1		۱-	100		I		
TABLE III—Continueu	ALKYLATION OF MONOALKYLMALONIC ESTERS, IN CALLOGETICAL ALKYLATION OF MONOALKYLMALONICS used unless otherwise indicated.)	3	Product Product (\$-picnylethyl)-	Dietity 53	Dictify (4-1) majorate	n.C. II, 0(CII2)2C((CII2)2C6115)(CO2C2II5)2		$C_6\Pi_6(G\Pi_2)_2(G\Pi_2C_6^{1.5}) = C_6\Pi_5(G\Omega_2C_2^{1.15})_2 = C_6\Pi_5(G\Pi_2C_6^{1.15})_3 = C_6\Pi_5(G\Pi_2C_6^{1.15})_3 = C_6\Pi_2C_6^{1.15}$	Dictivi (\$-plienylethyl)-(\$-eyelonexy-cthyl)malonate	[C <sub>6</sub> 11 <sub>5</sub> (C <sub>112</sub> ) <sub>2</sub> ] <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> 11 <sub>5</sub> ) <sub>2</sub>	Colls O(CH2)2 C(CH2)2 Colls (CO2C2H5)2	C6115 U(CH2)3 U(CH2CH5)(CO2C2115)2 C6H5 U(CH2)2 U(CH2CH5)(CO2C2H5)2	[Coliso(CII3)2]2C(CO2C3115)2 [Coliso(CII3)2]2C(CO2C3115)2	C2115.02.0C112.01.0C(C112.04.115)(CO2.02.115)2	p.CII3C6114CII2C(CII2CII=CII2)(CO2C2115/2	Diethyl methyl-(2-methoxy-3-	nitrobenzyl)maiouate z	malonate Trans.	p-cli30cgH4cH2cCcc2c2Hs/2	$c_{\rm H_2CH} = c_{\rm H_2}$	$c_2H_5o_2ccH_2c(co_2c_2H_5)_2$	CH.C.H.OCH.
	ALKYLATIO	(The and	Alkylating Agent	Cyclopentyl bromide	2.Cyclopentenyl chloride	Q <sub>8</sub> −Q <sub>9</sub>	n-C41190(CH2)2Cl 2-Methylcyclopentyl bromlde	C,115C112C1	ConsCH2Br p.Cyclohexylethyl bromlde		C <sub>6</sub> 11 <sub>5</sub> (C11 <sub>2</sub> ) <sub>2</sub> 13r	Colls O(CH2)3Cl	CoH,CH,CH,C	Broll, CO.C. H.	CellsCH2Cl	CII, CHCH 2DE	CH <sub>3</sub> I	$C_2\Pi_5I$	CII - CHCII, Br		T.CII CO.C.II.	DIOLIZATION CONTRACTOR
			į	C <sub>4</sub> 11 <sub>5</sub> (C11 <sub>2</sub> ) <sub>2</sub> (Cont.)	1								C,H,O(CH2)2		o-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub>	"CH,C,H,CIII	2-Methoxy-5-	nltrobenzy1	•	$p\text{-CH}_3\text{OC}_6\Pi_4\text{CH}_2$		

560	585	920 947	928	135 929	142 769 768	581 772	774 775, 374 374 755	412	412	616
Ethanol Ethanol	Ethanol	Ethanol Ethanol	Ethanol	Ethanol Ethanol	Ethanol Ethanol Toluene	CII,0II Ethanol	n-C <sub>3</sub> H <sub>7</sub> OH Ethanol — Ethanol Ethanol	Toluene	Tolucne	
NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> 11 <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	$NaOC_2H_5$	NaOC2H5 NaOC2H5	NaOC2Hs NaOC2Hs Na	NaOCII3 NaOC2Hs	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	ĸ	K NaOC,II,	, 1
11	ca. 70	1.1	l	<del>*</del>   8	8 4 8	មិន ដ	38118	72	68-70 86	
Diethyl ethyl(piperonyl)malonate Diethyl allyl(piperonyl)malonate	CH2CH2C(C31119-11)CO2.C2115	$CH_2 = CHCH_2(C_6^{11}_{19}-n)(CO_2C_2H_5)_2$ Diethyl (cyclobutylmethyl)-n-nonvlundorate	Diethyl n-nonyl-[\(\beta\)-(2-cyclopentenyl)ethyl}-malonate	n-C <sub>16</sub> H <sub>32</sub> C(C <sub>9</sub> 11 <sub>19</sub> -n)(CO <sub>2</sub> C <sub>2</sub> 11 <sub>5</sub> ) <sub>2</sub> Diethyl di-(y-cyclohexylpropyl)malonate C H (CH ) C(C 11 - NCO C H )	C <sub>6</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CH <sub>2</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>3</sub> C(CH <sub>3</sub> ) <sub>3</sub> C(CO <sub>3</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>3</sub> C(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> C(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> C(CO <sub>3</sub> C(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> C(CO <sub>3</sub> C(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> C(CO <sub>3</sub> C(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> C(CO <sub>3</sub> C(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> C(CO <sub>3</sub> C(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>3</sub> C(CO <sub>3</sub> C(CO <sub>3</sub> C(CO <sub>3</sub>	C <sub>6</sub> H <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>2</sub> O(CH <sub>3</sub> ) <sub>3</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub> ) <sub>2</sub> C <sub>7</sub> H <sub>2</sub> O(CH <sub>3</sub> ), CC <sub>7</sub> C <sub>7</sub> H <sub>3</sub> , CC <sub>7</sub> C <sub>7</sub> H <sub>2</sub>	$\{G_{0}H_{3}(C)G_{1}H_{3}H_{3}(C)G_{1}G_{2}H_{3}\},\\ G_{0}H_{3}(C)G_{1}H_{3}(C)G_{2}G_{3}H_{3},\\ G_{0}H_{3}CH_{2}(C)G_{1}H_{3}(C)G_{2}H_{3}\},\\ G_{0}H_{3}CH_{2}(C)H_{3}H_{3}(C)G_{2}H_{3},\\ m.CH_{3}C_{0}H_{4}(C)H_{3}H_{3}(C)G_{2}C_{2}H_{3})_{2}$	$_{\rm CH_2CH=CCICH_3}^{\rm CH_2CH=CCICH_3}$ Diethyl eyelopentyl- $_{\rm P}^{\rm H}$ -(m-methoxypheny)ethyl)malonate	Diethyl 2-cyelopentcnyl-[ $\beta$ -( $m$ -methoxy-phenyl)ethyl]malonate CH <sub>3</sub> CC=CHCH <sub>2</sub> C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	$(CH_2)_2C_6H_4CH_3^{-p}$
$C_2H_5Br$ $CH_2=CHCH_2Br$	$C_2-C_{16}$ $CH_2 \longrightarrow CH_2$	$CH_2 = CUCH_2Dr$ Cyelobutylmethyl bromíde	heta-(2-Cyclopentenyl)ethyl bromide	$n$ -C <sub>16</sub> 11 <sub>33</sub> I $\gamma$ -Cyelohexylpropyl bromide $n$ -C. H. Rr	Conscionation Co	C1-C9 CH31 C2H61 n-C3H,1	$C_6H_5^{\circ}O(CH_2)_3Dr$ $C_2H_5I$ $C_2H_5Br$ $C_4H_5Dr$ $CH_5CCI = CHCH_2CI$	Cyclopentyl bromide	2-Cyclopentenyl chloride CH3CCl≕CHCH2Cl	
Piperonyl	$G_{f 0}$ $n ext{-}C_{f 0}H_{f 10}$			y-Cyclohexylpropyl		$C_6 H_6 O(CH_2)_3$	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>5</sub> OH==CHCH <sub>2</sub> m·CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> (CH <sub>2</sub> ) <sub>2</sub>	$m ext{-}\mathrm{CH_3OC_6H_4(CH_2)_2}$	$p\text{-}\mathrm{CH}_3\mathrm{C}_6\mathrm{H}_4(\mathrm{CH}_2)_2$	,

Note: References 577-1080 are on pp. 322-331,  $\ddagger$  The halogen was not specified.

TABLE III-Continued

Alkylation of Monoalkylamensia Esters,  $\mathrm{RCH}(\mathrm{CO}_2\mathrm{R})_2$  (The diethyl ester was used unless otherwise indicated.)

	,	The same of the sa				
71	Alkylating Agent	Product	Yleld,	Ваяс	Solvent	Refer- ence
C10 n-C10H11	C1-C16	C112CH3C(C10H21-11)CO2C2H3	ca. 70	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	65
	`0' CH <sub>4</sub> =: CHCH <sub>4</sub> 4tr Cyclolutylmethyl bromide	$0 \longrightarrow 0$ $CII_3 = CIICII_2 C(C_{10}II_{21} \cdot n)(CO_2C_2II_3)_2$ $Diethy! (eyelobutylmethyl) \cdot n.$	1.1	$N_{\Lambda}OC_2H_S$ $N_{\Lambda}OC_2H_S$	Ethanol Ethanol	920,713
	p.(2.Cyclopentenyl)othyl	decylmalonate Dicthyl n-decyl-[h-(2-cyclopentenyl)ethyl}-	ł	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	928
	bromkle n-C <sub>10</sub> H <sub>21</sub> NF n-C <sub>13</sub> H <sub>25</sub> Nr-KI n-C <sub>1-H</sub> <sub>23</sub> I n-C <sub>1-H</sub> <sub>33</sub> I	undlonate (n.C <sub>10</sub> 11 <u>17</u> 12(CO <sub>5</sub> C <sub>2</sub> II <sub>5</sub> )2 n.C <sub>11</sub> II <sub>15</sub> (CC <sub>10</sub> II <sub>1</sub> -11)(CO <sub>3</sub> C <sub>2</sub> II <sub>5</sub> )2 n.C <sub>14</sub> II <sub>15</sub> (CC <sub>10</sub> II <sub>1</sub> -11)(CO <sub>3</sub> II <sub>1</sub> )1 n.C <sub>14</sub> II <sub>15</sub> (CC <sub>10</sub> II <sub>1</sub> -11)(CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub> )2	75 70 79	NaOC, II.5 NaOC, II.5 NaOC, II.5 NaOC, II.5	Ethanol Ethanol Ethanol Ethanol	951 70 135
Br(CH <sub>2</sub> ) <sub>10</sub> 3,7-Dimethyloetyl Citronelly(==C <sub>10</sub> H <sub>19</sub> )	CH <sub>3</sub> I CH <sub>4</sub> =CHCH <sub>2</sub> Br Cyclopentyl bromide	Br(CIL2) <sub>10</sub> C(CIL3)(CO <sub>2</sub> C <sub>2</sub> IL <sub>2</sub> ) <sub>2</sub> Diethyl allyl-(3,7-dimethyloetyl)malonato Diethyl cyclopenlyl(detronellyl)malonate	00   02	NaOC <sub>2</sub> H <sub>S</sub> Na	Ethanol Xyleno Xyleno	788 743 31
$\text{Geranyl}(\approx\!C_{10}\Pi_{17})$	n.Call, Br CH, — CH;	#-U,	ca. 70	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	282
C,U,(CH <sub>2</sub> ), C,U,(CH <sub>2</sub> ), C,U,(CH <sub>2</sub> ),	`O' Cyclopentyl bromide Cyffylir Cffyl	OCO Dictiyl eyelopentyl(geranyl)malonate C <sub>4</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>1</sub> C(C <sub>2</sub> H <sub>3</sub> )(CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>4</sub> H <sub>3</sub> CH <sub>2</sub> SCH <sub>2</sub> C(CH <sub>3</sub> )C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	60 1 52	Nn NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Xylene Ethanol Ethanol	31 755 794
CH <sub>2</sub> a-Naphthyl p-Naphthyl	C₁Ույ ԵՈւ₁≔ԵՈՐԵՈւրթ	Dimethyl cthyl-(x-napithyl)malonate* Diethyl allyl-(p-napithyl)malonate	40	NaOCH <sub>3</sub> NaOC <sub>2</sub> H <sub>5</sub>	CH3OII Ethanol	376 952

$c_{11}$	$C_{2}$ - $C_{7}$			1		000
$^{n ext{-}C_{11} ext{H}_{23}}$	CH <sub>2</sub> —CH <sub>2</sub>	CH <sub>2</sub> CH <sub>2</sub> C(C <sub>11</sub> H <sub>23</sub> -n)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> c	ca. 70	NaOc <sub>2</sub> H <sub>5</sub>	Ethanol	7.87
	CH. = CHCH.Br	CH. = CHCH. C(C,, H.,-n)(CO,C,H <sub>5</sub> ),	l	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	920
	Cyclobutylmethyl bromide	Diethyl (cyclobutylmethyl)-n-undecyl-	1	NaOC2H5	Ethanol	947
	$\beta$ -(2-Cyclopentenyl)ethyl	Diethyl n-undeeyl- $[\beta$ -(2-cyclopentenyl)-	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	928
	bromldo	ethyl]malonate	â	NaOC.H.	Ethanol	135
n-C,H,,CH(CH,)	n-Ci, H. Br-NaI	n-C,H,,CH(CH,)C(C,+H,s-n)(CO,C,H,),		Na	Xylene	20
C,H's(CH3),	C,H,Br	C,H,(CH,),C(C,H,)(CO,C,H,),		NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	755
2-p-Cymylmethyl	chj	Diethyl methyl-(2-methyl-5-iso-	20	Na	CeHe	808
	CH <sub>3</sub> I	propyroenzylmalonace Diethyl methyl-(2-methyl-5-iso-	20	NaOC <sub>2</sub> H <sub>S</sub>	Ethanol	418
1-Naphthylmethyl	$CH_2 = CHCH_1X_1$	propylbenzyl)malonate Diethyl allyl-(1-naphthylmethyl)malonate	ı	NaOC <sub>2</sub> H <sub>5</sub>	Toluene	512
(11-13)	$ heta ext{-}B$ romomethylnaphthalene	Diethyl (1-naphthylmethyl)-(2-	ı	1	1	945
2-Naphthylmethyl $(=C_{11}H_{13})$	CH <sub>2</sub> =CHCH <sub>2</sub> Br	naphthylmethyl)malonate $CH_2 = CHCH_2C(C_{11}H_{13})(CO_2C_2H_5)_{\frac{1}{2}}$	I	$NaOC_2H_{\mathcal{S}}$	Toluene	513
$C_{12}$						
$n \cdot \mathbf{C}_{\mathbf{12H_{25}II}}$	$C_2H_5X\eta\eta$	n-C <sub>11</sub> H <sub>2</sub> ,C(C,H <sub>4</sub> )(CO,C,H <sub>4</sub> ),	١	I	ı	783
	CH <sub>2</sub> = CHCH <sub>2</sub> Br	CH3=CHCH2C(C12H25-n)(CO2C2H5)2	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	920
	$\mathcal{O}_{\mathcal{C}}$ objective $\mathcal{O}_{\mathcal{C}}$ of $\mathcal{O}_{\mathcal{C}}$ o	Diethyl (cyclobutylmethyl)-n-dodecylmalonate Diethyl n-dodecyl-[\$-(2-cyclopentenyl)-		NaOC2Hs NaOC2Hs	Ethanol Ethanol	947 928
$C_6H_5(\mathrm{CH}_2)_6$	$n$ - $\zeta_{16}H_{33}$ I $\zeta_{2}H_{5}B_{5}$	r-C <sub>16</sub> H <sub>33</sub> C(C <sub>12</sub> H <sub>25</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>6</sub> C(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	88	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	Ethanol Ethanol	135 755
Note: References 57	Note: References 577-1080 are on nn 300 301					

· The dimethyl ester was used in this experiment. Acke: References 577-1080 are on pp. 322-331.

The halogen was not specified. IThe order of introduction of the alkyl groups was not stated.

TABLE 111-Continued

Alkylation of Monoalkylmalonic Estens, RyCH(CO<sub>2</sub>R)<sub>2</sub> (The dictityl ester was used unless otherwise indicated.)

Refer-	enco	683	953 546	510	517	110	128	514	960	938	919	224 156, 954	224	150 516	520		
	Solvent	Ethanol	Ethanol	Ethanol	Ethanol Ethanol	Ethanol	Xylene	Toluene		Ethanol Ether	Ethanol Calla	Toluene Ether	C, II,	Colli	Ethanol		
(.bo.	Ваяв	NaOC <sub>2</sub> IIs	NaOC,IIs	NAOC II.	NaOC,113	NaOC <sub>2</sub> IIs	Na	NaOC <sub>2</sub> II <sub>3</sub>		NaOC,II's	Na NaOC <sub>2</sub> H <sub>3</sub>	Na Na	of enolate	Na Na	NaOC,H,		
ndicat	Yleld,		ţ			82 83 88 83	i	i		i	۲ <del>۲</del> کا کا کا	2 3	80	원 원	15	2	
ALKYLATION OF MUNICIPAL unless otherwise indicated.)	g diethyl ester was many	Product	C1,1I1,C(C11,)(CO4C2115)2	GDII, ((CIL) ((O2C115)3	C1111.C(C113.00-51.11.50 C1111.C(C11.011=01.1.00.1.1.3)	$C_{14}\Pi_{11}C(C_{11}\Pi_{2}^{*}\Pi_{31}C_{22}\Pi_{3}^{*})$ $C_{14}\Pi_{12}C(\Pi_{12}\Pi_{12}^{*}(C_{14}\Pi_{13}^{*})C_{22}C_{31}\Pi_{32}^{*})$	(H11CC1=CHCH1C(C11TH)	plethyl methyl-(2-methyl-1- naphthylmethyl)malonate	Dictivi allyt-(4-metay) napitthyfmethyf)malonate	(II.3 63v- ** ***	$CH_2 = CHCH_2 (CC_{13}H_3)^{-H}(CC_{23}H_2)^{2}$ $(C_6H_3)_2 CHC(CH_3)(CO_2G_3H_3)^{2}$ $(C_6H_3)_2 CHC(CH_3)^{2}$	(C <sub>6</sub> H <sub>5</sub> ), CHC(CH <sub>2</sub> CH), (C <sub>6</sub> H <sub>5</sub> ), (C <sub>6</sub>	[(C,II,3),CIII,C(C,2,2,11,3), [(C,II,3),CIII],C(CO,2,C,III,3),2	(10,11),C11),C(CO,C,11s)(CO,C11(C,11s))†††	(p-611,5211,2011C[G11(G <sub>6</sub> 11,5)3 (CO <sub>2</sub> C211,5)2 (p-611,5211,1,2011C[G11(G <sub>6</sub> 11,5)3 (CO <sub>2</sub> C211,5)2 (p-611,51,511,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1	$CII_1CCI = CIICII_2C(C_{13}II_{13}O)(CO_2C_2^{-11}_3)_2$	
ALKYL	ATT)	Alkylating	I II		C111511 C2115111	F.C.11, 15.11.	11,001 - 011011,00 11,001 - 011011,01		$CH_3 = CHCH_2^{1/2}$		CII, T CIICII BE	CH <sub>2</sub> <sup>1</sup> CHCH <sub>2</sub> <sup>1</sup> Br	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CHBr (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CHBr	((,0113)2(111)1	(C,115);CHBr (p-CH;C,114);CHCl	$CH_1 = CHCH_2 Br$ $CH_2 CCI = CHCH_2 CI$	
			, <sub>2</sub>	A.1Naphthylethyl			factories and	C Craffin)	methyl 1. naphthyl-	methyl	C13 n-C3,113	(Calis)2CH				9.Fluorenyl g.(5.Methoxy-1-	naphthyl)ethyl (-= C12II 13O)

	nol 920 ene 515		nol 955	nol 955		207	nol 207	207			r 156	1100	7	101 104 011 86,956	
	NaOC <sub>2</sub> H <sub>5</sub> Ethanol NaOC <sub>2</sub> H <sub>4</sub> Toluene		NaOC2Hs Ethanol	NaOC <sub>2</sub> II <sub>s</sub> Ethanol		Na C <sub>6</sub> II <sub>6</sub>	NaOC <sub>2</sub> H <sub>5</sub> Ethanol	n C <sub>e</sub> H	NaOC <sub>2</sub> II <sub>5</sub> Ethai	a Colum	BrMg salt‡‡‡ Ether	of enough Na C <sub>6</sub> H <sub>6</sub> BrMg salt±± Ether	•	Mg(OCH <sub>3</sub> ) <sub>2</sub> CH <sub>3</sub> OH	
	22 		61 N	82 N		25 N	76 N	7. 	18	0 <del>,</del>	₩	80 N	, ,-	i	
	$CII_2 = CII CH_2 C(C_{14}II_{29} \cdot n)(CO_2 C_2 II_5)_2$ Diethyl allyl-(4-lsopropyl-1-	naphthylmethyl)malonate	$C_{14}\Pi_9C(C_3\Pi_7-n)(CO_2C_2\Pi_5)_2$	$\mathrm{C}_{14}\mathrm{H_6C(CH_2CH}=\mathrm{CH_2)(CO_2C_2H_5)_2}$		Tetracthyl x-methyl-d-phenyl- butane-x,a,β,γ-tetraearboxylate	Tetracthyl α-methyl-δ-phenyl- hutanga α β actotrogenaction	Collscit_coll(CH3)CONH2	$\left( C_6\Pi_5 \text{CH}_2 \text{CC}\Pi_3 \right) \left( C_9 \Gamma_5 \Pi_5 \right)_2 \\ \left( C_6\Pi_5 \text{CH}_2 \text{CH} - \text{CHC} \text{CC} \Pi_3 \right) \left( \text{CO}_2 C_2 \Pi_5 \right)_2 \right.$	(p-CH <sub>2</sub> C <sub>6</sub> H <sub>3</sub> )CHC(CH <sub>6</sub> H <sub>3</sub> )CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> )	(7:-C113C6114)2C11C[C11(C6115)2](CO2C2115)2	$\{(p\text{-}\mathrm{CH}_3C_6H_4)_2\mathrm{CH}\}_2C(\mathrm{CO}_2C_2H_5)_2$ $\{(p\text{-}\mathrm{CH}_3C_6H_4)_2\mathrm{CH}\}_2C(\mathrm{CO}_3C_3H_5)_3$	Conscilication Constitution Con	II,C.CH-CHCOC,II,	C(CO2,CH3)2.
	$CH_2 = CHCH_2Br$ $CH_3 = CHCH_3Br$	7	$n$ - $C_3H_7I$	CII2=CIICH2Br		сп,1	сп <sub>3</sub> г	CH <sub>3</sub> I	спат	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CHBr	10112/3/1101	$(p\text{-}\mathrm{CH}_3C_6\mathrm{H}_4)_2\mathrm{CHCl}$ $(p\text{-}\mathrm{CH}_3C_6\mathrm{H}_4)_2\mathrm{CHCl}$	CH <sub>3</sub> I	None	
$c_{14}$	$n$ - $C_{14}H_{29}$ 4-Fouronyl-1-	naphthylmethyl	9-Phenanthryl	(	$C_{15}$	$C_6H_5CH_2CH$ - $(CO_2C_2H_5)CH$ - $(CO_3C_3H_5)$	4	‡:	<b>=</b>	$(p \cdot \mathrm{CH_3C_6H_4})_2\mathrm{CH}$			CeH5COCH2CH(CeH5)	Cells COCHBrCH(Cells) low and high	melting isomers

Note: References 577-1080 are on pp. 322-331.

. The dimethyl ester was used in this experiment.

†† The ester alkylated in this experiment was  $C_6H_5\mathrm{CH}_2\mathrm{C}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2\mathrm{CH}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)\mathrm{CH}_2\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5.$ 

\*\*\* The bromomagnesium salt of the enolate was derived from the addition of phenylmagnesium bromide to dictivy benzylidenemalonate. ††† Benzhydryl ethyl benzhydrylmalonate was used in this experiment.

\*\*\* The bromomagnessum salt of the enolate was derlyed from addition of p-tolyimagnesium bromido to p-methylbenzylidenemalonate.

TABLE III—Continued

Refer-	ence 85	88	88	85
	Solvent CH3OH	СИ3ОИ	сп,0н	сизон
$({ m CO}_2{ m R})_2$ ted.)	Base KOCOCH3	$ m Mg(OCH_3)_2$	кососи,	${ m Mg(OCH_3)_2}$
rrs, R'CH rwise indice	Yleld,	1	100	100
Alikylation of Monoalkylamalonic Esters, R'CH(CO $_2{\rm R})_2$ (The diethyl ester was used unless otherwise indicated.)	Product II, C, C, II—C, II CO C, II , Ibr-?	Q(CO <sub>2</sub> CH <sub>2</sub> ).* (both isomers) II <sub>5</sub> C <sub>6</sub> CH——CHCOC <sub>6</sub> II <sub>4</sub> Br-p	QCO <sub>2</sub> CH <sub>3</sub> )2* (both Isomers) m-O <sub>2</sub> NH <sub>4</sub> C <sub>6</sub> CH—CHCOC <sub>6</sub> H <sub>5</sub>	$\begin{array}{c} C(\mathrm{CO}_2\mathrm{CH}_3)_2^* \\ (\mathrm{both \ isomers}) \\ m \cdot \mathrm{O}_2\mathrm{NH}_4\mathrm{G}_6\mathrm{CH} - \mathrm{CHCOG}_6\mathrm{H}_5 \end{array}$
	~	None None	None	None
	ដ	p-BrC <sub>6</sub> II <sub>4</sub> COCIIBr- CII(C <sub>6</sub> II <sub>6</sub> ) (both isomers)	The driver	C <sub>a</sub> H <sub>3</sub> OOOHMOA (C <sub>a</sub> H <sub>4</sub> NO <sub>2</sub> -m) (both Isomers)

C <sub>18</sub>	$C_1$ - $C_{16}$					
n-C1,H.	CH,1	$n$ - $C_{16}H_{33}C(CH_3)(CO_2C_2H_5)_2$	I	Na	Xylene	629
3	00°(0°11'0)	n-C10H33C(C,H9-n)(CO2C,H9)2\$\$\$	83	NaOC, III, n	$(n-C_4\Pi_00)_2CO$	330,800
	$c_{\rm s} n_{\rm s} c n_{\rm s} c n_{\rm s}$	$n$ - $C_{16}H_{33}C(CH_2C_6H_5)(CO_2C_2H_5)_2$	67	KOC <sub>2</sub> H <sub>5</sub>	(C2H5O)2CO	#
	Censon co	n-C161133C(CH2C6H5)(CO2C4H9)2\$\$\$	67	KOC,Hg-n	$(n \cdot C_4 \Pi_9 0)_2 C 0$	51, 227
	n-C <sub>6</sub> II <sub>17</sub> I	$n \cdot C_{16} II_{33} C(C_{6} II_{17} \cdot n)(CO_{2} C_{2} II_{5})_{2}$	l	$NaOC_2H_5$	Ethanol	134
	n-CleH33Br	$(n \cdot C_{16}11_{33})_2 C(CO_2 C_2 11_6)_2$	<b>f</b> ·9	Na	Xylene	679,957
	$n$ - $C_{16}$ $\Pi_{33}$ $Br$	$(n - C_{16}H_{33})_2C(CO_2C_2H_5)_2$	i	$NaOC_2\Pi_{\delta}$	Ethanol	841
C, II, COCHBrCII	None	C, II, COCII—CII——	53	кососи,	си,оп	953
OCH <sub>3</sub>		C(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> *		,	,	
$\sigma_{\Gamma_{7}}$						
$n$ - $C_{17}$ $H_{35}$	$_{ m II}$	$n\text{-}\mathrm{G}_{17}\mathrm{H}_{15}\mathrm{C}(\mathrm{CH}_3)(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	1	Na	Toluene	<del>4</del> 00
$C_{23}$	* A.V.					
3-Decytridecyl	CH31	Diethyl (3-decyltridecyl) methylmalonate	i	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	20
Note: References * The dimethyl est §§§ The di-n-butyl	Note: References 577–1080 are on pp. 322-331. * The dimethyl ester was used in this experiment. §§§ The di-n-butyl ester was used in this experiment	ن ن				

$(C_2H_5O_2C)_2CH$ -	${ m Br_2}~{ m or}~{ m I_2}$	Tetraethyl 3-ethyleyelopropane-	I	Na	Ether	87
$\mathrm{CH}(\mathrm{C_2H_5})\mathrm{CH}(\mathrm{CO_2C_2H_5})_2$	$c_2 \pi_5 I$	$1,1,2,2$ -retracarboxylate $(C_2H_5O_2C)_2C(C_2H_5)$ CH $(C_2H_5)$ C	1	$Na0C_2H_5$	Ethanol	87
(C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C) <sub>2</sub> CHC(CH <sub>3</sub> ) <sub>2</sub> -	Dr <sub>2</sub>	C(C2 H5)(CO2C2 H5)2 None	1	Na	Ether	87
$CH(CU_2C_2H_5)_2$ $(C_2H_5O_2C)_2CBrC(CH_3)_2$ -	None	Tetractly1 3,3-dimethyleyelopropane-	1	ип,	си зон	87
$_{\mathrm{CH}(\mathrm{CO_2C_2H_6})_2}^{\mathrm{CH}(\mathrm{CO_2C_2H_6})_2}$	CH <sub>3</sub> I	1,1,2,2-retracarboxylave $(C_2 H_5 O_2 C)_2 C(C H_3) C H == C(C O_2 C_2 H_5)_2$	I	$NaOC_2H_5$	Ethanol	221
on = 0,00202n5/2	C,H5CH2CI	(C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C) <sub>2</sub> C(CH <sub>2</sub> C <sub>6</sub> U <sub>5</sub> ).	72-84	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	221, 231
(C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C) <sub>2</sub> CBr-	None	Tetracthyl 3-phenylcyclo-	I	$^{ m NH_3}$	сизоп	87
$(C_2H_5O_2C)_2CH_5)_2$ $(C_2H_5O_2C)_2CH(CH_2)_2$ -	CH <sub>3</sub> I	propune-1,1,2,2-retractivoxymite $(C_2H_5O_2C)_2C(CH_3)(CH_2)_2$ .	85	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	003
011(00202115/2	$\mathrm{CH_2L_2}$	Tetracthyl eyelopentane-	1	$\mathrm{NaOC_2H_5}$	Ethanol	301,302
	$C_2\Pi_5I$	(C <sub>2</sub> 11 <sub>5</sub> O <sub>2</sub> C) <sub>2</sub> C(C <sub>2</sub> H <sub>5</sub> )(CH <sub>2</sub> ) <sub>2</sub> -	65	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	000
	$\mathrm{Br}(\mathrm{CH}_2)_2\mathrm{O}(\mathrm{CH}_2)_2\mathrm{Br}$	Tetractiyl octamethylene-	17	$\rm Mg(OC_2 H_5)_2$	Ethanol	219
$(C_2H_5O_2C)_2CH(CH_2)_3$ -	$(C_2H_5O_2C)_2CBr(CH_2)_2CBr(CO_2C_2H_5)_2$ $CH_3I$	Oxuce-4,4,1,7-tetracarboxymuc Cyclobutane-cis-1,2-dicarboxylle acid (C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C/2H <sub>3</sub> )(CH <sub>3</sub> ) <sub>3</sub> -	1-1	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>3</sub> H <sub>5</sub>	Ethanol Ethanol	261
$\mathrm{CH}(\mathrm{CO_2C_2H_5})_2$	$ ext{CH}_2 ext{L}_2$	C(CH <sub>3</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> Tetraethyl eyelohexane-	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	299
	$C_2U_5I$	$(C_3H_5O_2C)_2C(C_2H_5)(CH_2)_3$	1	$NaOC_2H_5$	Ethanol	303
	n-C <sub>3</sub> H <sub>7</sub> I	C(C <sub>2</sub> H <sub>5</sub> O' <sub>2</sub> C' <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> (C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C) <sub>2</sub> C(G <sub>3</sub> II <sub>3</sub> -n)(GII <sub>2</sub> ) <sub>3</sub> - C(C H -2/CO C H )	1	$NaOC_2H_5$	Ethanol	303
	i-C <sub>3</sub> H,I	$(C_2H_5O_2^*C_3H_7^{-18}(C_2H_5)_2$ $(C_2H_5O_2^*C)_2(C_3H_7^{-18}(CH_2)_3^{-18}$ $(C_2H_5O_2^*C)_2(C_3H_7^{-18})_3^{-18}$	1	$\rm NaOC_2 II_5$	Ethanol	303
	i-C₄HgI	(C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C) <sub>2</sub> C(C <sub>4</sub> H <sub>6</sub> -i)(CH <sub>2</sub> ) <sub>3</sub> - C(C <sub>3</sub> H <sub>2</sub> O <sub>2</sub> C) C(C <sub>4</sub> H <sub>6</sub> -i)(CH <sub>2</sub> ) <sub>3</sub> -	1	${ m NaOC}_2{ m H}_5$	Ethanol	303
	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> Cl	(CH <sub>2</sub> O <sub>2</sub> C) <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> . (CH <sub>2</sub> O <sub>2</sub> C) <sub>2</sub> (CH <sub>2</sub> C <sub>4</sub> H <sub>3</sub> )(CH <sub>2</sub> ) <sub>3</sub> . (CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> U <sub>5</sub> ) <sub>3</sub> .	1	$NaOC_2H_\delta$	Ethanol	303

Note: References 577-1080 are on pp. 322-331. The structure of the product is uncertain.

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	Refer-	ence	8 8 8 8	215	58	63	63	63	63, 213 64	64	63	63 84	63	63	64	901 28	212	28	8 6 9 79 9 79	82,63	28	
		Solvent	Ethanol	Ethanol Rthanol	Ethanol	Toluene	Toluene	Toluene	Toluene	Toluene	Toluene	Toluene	Toluene	Tolueno	Toluene	Ethanol Fthanol	Ether	Ethanol	Ethanol	Ethanol	Ethanol	
	5)2	Base	NaOC2H5	NaOC <sub>2</sub> H <sub>5</sub>	NaOC2H5 NaOC2H5	NaNH2	NaNH	Nanh2 NaNH3	NaNH	NaNH	NaNH2	NaNH,	NaNH,	NaNH2 NoNH2	NaNH2	NaOC2H5	NaOC2H5	NoOC.H.	NaOC2H5	NaOC2H5	NaOC2H5 NaOC2H5	
,	702C2H,	1 lota, 0/.	51	35	76	88	81	50	2 8	Poor	Poor 59	40	61	50	30 Poor	80	75	1	67	43	59 21	
TABLE V	ALEXIDENEMALONIC ESTERS, R=C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>		Product	$CH_3CH = CHC(C_3H_1 - n)(CO_2C_2H_3)_2$	$\text{CH}_{\text{CH}}\text{CHC}(\text{C}_{2}^{1}\text{H}_{7}^{1})/\text{CC}_{2}^{2}\text{C}_{2}^{1}\text{S})_{2}$	CH,CH=CHC(C,H,,n)(CO,C,H,s)2	CH <sub>2</sub> =C(CH <sub>2</sub> )C(CH <sub>2</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub> );	CH <sub>2</sub> =C(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>5</sub> )(CC <sub>2</sub> C <sub>2</sub> F-3); CHC(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> ·n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> );	$CH_2 = C(CH_3)C(C_3H_7 \cdot i)(CO_2C_2H_5)_2$ $CH_2 = C(CH_3)C(C_3H_7 \cdot i)(CO_2C_2H_5)_2$	CH <sub>2</sub> =C(CH <sub>3</sub> )C(CH <sub>2</sub> CH=Ch <sub>2</sub> )(CC <sub>2</sub> C <sub>2</sub> C <sub>3</sub>	Structure not determined	$CH_2 = C(CH_3)C(C_4H_3 - n)(CO_2C_2H_3)$	$CH_2 = C(CH_3)C(C_4H_3^{-1})(CO_2C_2H_3)_2$ $CH_2 = C(CH_3)C(C_4H_3)^{-1}(CO_3C_2H_3)_2$	CH2=C(CH3)C(CH2CII-CZ-CZ-CZ)CH2CH2CH2CH2CH2CH2CH2CH2CH2CH2CH2CH2CH2C	CH <sub>2</sub> =C(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>11</sub> -i)(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>		-	CHCCCHC(CH;)(CO2C2H3)2	$C_2H_3CH=CHC(C_3H_7\cdot n)(CO_2C_2H_3)_2$	C2H,CH=CHC(C3H,-*)(CO2C2+15/2	C2H,CH=CHC(C4H,-n)(CO2C,H,s)	C2H CH=CHC(C4H3-sec)(CO2C2H5/2
	TIPA TERMA A	ALMINAT	Allering Agent	Alkymane-	i.C3H,I	CH2=CHCH2Br	n.C.H.J.SO,	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> SO <sub>4</sub>	n-C <sub>3</sub> H,Br	CH,=CHCH,Br	CH2=CCICH2CI	CH <sub>2</sub> —CBrCH <sub>2</sub> Dr	$h \cdot C_4 \Pi_{\mathfrak{g}}$	CH3CH=CHCH2Br	n-C <sub>5</sub> H <sub>11</sub> Br	C,H,CH=CHCH2Br	CHJ	$C_2H_{s,1}$	$(C_2H_5)_2SO_4$ $n_*C_2H_*Br$	¿C,H,Br	CH2=CHCH2Br	sec-Can Br
																	11					

$CH_3C(OC_2H_6)=$	$C_2H_\delta X^*$	$\mathrm{CH}_2\mathrm{=-C}(\mathrm{OC}_2\mathrm{H}_5)\mathrm{C}(\mathrm{C}_2\mathrm{H}_5)(\mathrm{CO}_3\mathrm{C}_2\mathrm{H}_5)_2$	20	$NaOC_2H_5$	Ethanol	203
	$C_2H_5X*$	$CH_2 = C(OC_2H_5)C(C_2H_5)(CO_2C_2H_5)_2$	09	NaOC4H9-t	HO"H"OH	203
	$n.C_3H,X^*$	$\mathrm{CH_2}$ ==C(OC <sub>2</sub> H <sub>5</sub> )C(C <sub>3</sub> H <sub>7</sub> -n)(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	72	NaOC <sub>3</sub> H <sub>7</sub> -i	$i$ - $C_3$ H $_2$ OH	203
	CH2=CHCH2X*	$CH_2$ = $C(OC_2H_6)C(CH_2CH$ = $CH_2)(CO_2C_2H_6)_2$	59	NaOC <sub>3</sub> H <sub>7-1</sub>	i-C3H,OH	203
	$n \cdot C_4 H_g X^*$	$\mathrm{CH}_{2}$ == $\mathrm{C}(\mathrm{OC}_{2}\mathrm{H}_{5})\mathrm{C}(\mathrm{C}_{4}\mathrm{H}_{5}-n)(\mathrm{CO}_{2}\mathrm{C}_{2}\mathrm{H}_{5})_{2}$	85	NaOC <sub>3</sub> H,-i	i.C <sub>3</sub> H,0H	203
	$i\text{-}\mathrm{C}_5\mathrm{H}_{11}\mathrm{X}^{\color{red}*}$	$CH_2$ — $C(OC_2H_5)C(C_6H_{11}-i)(CO_2C_2H_5)_2$	40	NaOC3H7-i	i-C3H,OH	203
$C_2H_3C(CH_3)=$	$(CH_3)_2SO_4$	$CH_3CH = C(CH_3)C(CH_3)(CO_2C_2H_5)_2$	92	NaNH,	Toluene	237
	$(C_2H_5)_2SO_4$	$CH_3CH = C(CH_3)C(C_2H_5)(CO_2C_2H_5)_2$	70	NaNH2	Toluene	237
	$n ext{-}C_3H$ ,Br	$\mathrm{CH_3CH} = \mathrm{C}(\mathrm{CH_3})\mathrm{C}(\mathrm{C_3H_7\text{-}n})(\mathrm{CO_2C_2H_5})_2$	65	NaNH,	Toluene	237
	CH2=CHCH2Br	$CH_3CH = C(CH_3)C(CH_2CH = CH_2)(CO_2C_2H_6)_2$	09	NaNH,	Toluene	237
1	n-C,H,Br	$CH_3CH = C(CH_3)C(C_4H_6-n)(CO_3C_2H_5)_2$	49	NaNH2	Toluene	237
1.C,H,CH=	$C_2H_5I$	$(CH_3)_2C = CHC(C_2H_5)(CO_2C_2H_5)_2$	40	NaOC,H,	Ethanol	28
n-C <sub>1</sub> II CH=	$C_2H_5Br$	$n \cdot C_3H$ , $CH = CHC(C_2H_5)(CO_2C_2H_5)_2$	09	NaOC <sub>2</sub> H	Ethanol	38
	n-C <sub>3</sub> H <sub>7</sub> Br	$n \cdot G_3H$ , $CH = CHC(C_3H \cdot \cdot \cdot n)(CO_2C_2H_5)_2$	65	NaOC2H5	Ethanol	28
# 00% #D	1.C3H,I	$n \cdot C_3H_1CH = CHC(C_3H_7 \cdot i)(CO_2C_2H_5)_2$	70	NaOC2H,	Ethanol	28
CH <sub>3</sub> C(OC <sub>3</sub> H <sub>7</sub> ·n)=	CH2X*	CH2=C(OC3H7.n)C(C2H5)(CO2C2H5);	39	NaOC3H7-1	:C3H,OH	203
#HO 11 0.1	CH <sub>3</sub> I	··C,H,CH=CHC(CH,)(CO,C,H,),	93	NaOC2H5	Ethanol	58
	CH.C.	1-C <sub>3</sub> H,CH=CHC(C <sub>2</sub> H <sub>5</sub> )(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	88	NaOC,H,	Ethanol	28
	"Canabr	$v \cdot C_3 H, CH = CHC(C_3 H, -n)(CO_2 C_2 H_{\epsilon})_2$	98	$NaOC_3H_5$	Ethanol	88
	CH — CHOR D.	1-C,H,CH=CHC(C,H,-i)(CO,C,H,),	86	NaOC <sub>2</sub> H	Ethanol	80
"-Callmerte :	CII.I	1-Cat, CH=CHC(CH, CH=CH_)(CO, CaH,).	35	NaOC,H,	Ethanol	215
	C,11,13;	"City of the CHC(CH3)(CO,C,H3),	85	NaOC,H,	Ethanol	8
18.4.1.1.12.14.1	いまべき	$h \cdot c_1 u_0 \text{CH} = \text{CHC}(C_1 H_2)(\text{CO}_2 C_1 H_3)_2$	58	NaOC,H,	Ethanol	o o
_	* 7. 11. 1.	(11 - (100) - 1 - (100) - 1 - (100) - 1 - (100) - (1	Ťi	NaOC,H;	1-C.H.OH	903
Never References 37	Note: References 377-1080 are on me one	(1.1 - 1.1 -	55	NaOC,H,-;	i-C,H,OH	208
"The halogen was not specified	int specified.	, see .			-	)

#### TABLE VI

Alkylation of Cyanoacetic Esters,  $\mathrm{CH}_2(\mathrm{CN})\mathrm{CO}_2\mathrm{R}$ (The othyl ester was used unless otherwise specified.)

Refor-	onco	270	271, 272		962 568, 963	185	304 964, 586 965, 966,	967	964 589, 590, 591	590, 591	590, 591	39	968	
	Solvent	Ethor	Ethor		Ethor Ethanol	Ether	CH <sub>2</sub> OH Ethanol		Ethanol Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	
ı	Raso	No	Na		Na NaOC2Hs	$N_{0}OC_{2}H_{5}$	$NaOCH_3$ $NaOC_2H_5$		NaOC2Hs NaOC2Hs	NoOC.H.	NaOC <sub>2</sub> H <sub>5</sub>	NaOC2H 5	$NaOC_2H_5$	
	Yield,	۱ ۶	i		122	12	12		60			28	ន	
(The ethyl ester was used		Product	Tricthyl 1,2,3-tricylanocyclop, cym. 1,2,3-tricarboxylato	C,H,O,CCH(CN)CH(CN)CO,C,C,C	CH3CH(CN)CO,C2,H5	$(\operatorname{CH}_i(\operatorname{CN}) \circ \operatorname{OL}_i \circ_i H_s) $ $(\operatorname{CH}_i)_k \circ (\operatorname{CN}) \circ \operatorname{OL}_i \circ_i H_s)$	CH,CH(CN)CO,C,H,s CH,O,CCH(CN)CH==C(CN)CO,CH,*	C <sub>2</sub> H <sub>6</sub> O <sub>2</sub> CCH(CN)CHI-O(C <sub>2</sub> -2	$C_2H_5O_2CCH(CN)CH==C(CN)CO_2C_2H_5$ $C_2H_2O_2CC(N_0)(CN)CH==C(CN)CO_2^2C_2^2H_5$	7 6 47	$C_2H_2O_2CCH(CN)CH(CN)CO_2C_2H_5$ $C_2H_3O_2CCH(CN)CH(CN)CO_2C_2H_5$	H.OOVNOIHO H OL	(C2H5)2C(CN)CO2CH3*	2,H,5CO(VO)\CO(\C) (C,H,5)
		Alkylating Agent	I.s.	$I_2$	$G_1$	CH <sub>3</sub> I	CH <sub>3</sub> I CHCl <sub>3</sub>	CHCI3	CHI	, coi	CBr <sub>4</sub> CCl <sub>3</sub> NO <sub>2</sub>	$C_2$	$\mathrm{C_2H_5Br}$	$C_2H_5Br$

			1		. 1.3	ault.	LLATION	i U	r 158.	EISK	S AND	NII	KILES	:
169	185 95, 963	95	249	540	696	970 309, 479	310		971, 972, 973	38, 963	562 288	240 568, 225,	963 962, 963	icd as tho cyclo-
Ethanol Ether	Ethanol	Ethanol	Ethanol	Ethanol	Ether	Ethanol	Ethanol		Ethanol	Ethanol	Ethanol Ethanol	Ethanol	Ether	It was later identif
NaOC <sub>2</sub> H <sub>5</sub> Na	NaOC <sub>2</sub> H <sub>5</sub>	NaOC,H,	NaOC,H,	NaOC <sub>2</sub> H <sub>5</sub>	8 N	NaOC <sub>2</sub> H <sub>5</sub>	NaOC,H,		NaOCHE	NaOC, H,	NaOC,H, NaOC,H,	NaOC <sub>2</sub> H <sub>5</sub>	Na	o (ref. 697).
93 1 8	£ 75	30	75	09	1	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	1 1		ca. 63	49	70 54 65	63	20	iovalerat
(O,H,),C(CN)CO,C,H, C,H,CH(CN)CO,C,H, C,H,CH(CN)CO,C,H,	C <sub>2</sub> H <sub>3</sub> CH(CN)CO <sub>3</sub> C <sub>2</sub> H <sub>3</sub>	$(C_2H_5)_2C(CN)CO_2C_2H_5$ C H CH/CN/CO C H	Carts CH (CN) CO2 CaH s	CH, OCH, CH (CN) CO, C, H	C.H.O.CCHICANCH.N.CHICANCO C.H.	Ethyl 1-cyanocyclopropane-1-carboxylato	I-carboxylate‡ Ethyl I-cyanocyclopropane-1-carboxylate, diethyl α,α'-dicyanoadipato, and othyl	2-mmo-3-cyanocyclopentano-1-carboxylato	n-C <sub>3</sub> H,CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> (n-C <sub>3</sub> H,),2(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	$\{n\text{-}\mathrm{C}_2\mathrm{H},\mathrm{CH}(\mathrm{CN})\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5$ $(n\text{-}\mathrm{C}_3\mathrm{H}_7)_2\mathrm{C}(\mathrm{CN})\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5$	(n·C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> C(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> CH <sub>5</sub> S(CH <sub>2</sub> ) <sub>2</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> i·C <sub>3</sub> H,CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	$\left\langle i\cdot C_3H_7CH(CN)CO_2C_2H_5 \right\rangle$	((i.C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> C(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> CH <sub>2</sub> ==CHCH <sub>2</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> 0 are on pp. 322–331.	Then originally isolated this product was formulated as othyl α,δ-dicyanovalerato (ref. 697). It was later identified as tho cyclo- miane derivative indicated (ref. 712).
.C <sub>2</sub> H <sub>5</sub> Br C <sub>2</sub> H <sub>5</sub> I C <sub>2</sub> H <sub>5</sub> I	CH,I	C2H 5.1 (C.H 11.80)	(Czr. 5)2 O4 (C.H. 5)SO.	CH <sub>3</sub> OCH <sub>2</sub> Cl	CH,CICH,CI	CH <sub>2</sub> BrCH <sub>2</sub> Br	$\mathrm{CH_2BrCH_2Br}$	C <sub>3</sub>	$n ext{-}\mathrm{C}_3\mathrm{H}_7\mathrm{Br}$	n-C <sub>3</sub> H,I ,, C H I	$^{\prime\prime\prime}$ :C <sub>3</sub> H,1 CH,SCH <sub>2</sub> CH,CI.KI $^{\prime\prime}$ :C <sub>3</sub> H,Br	.c,H,I	CH <sub>2</sub> =CHCH <sub>2</sub> I  CH <sub>2</sub> =CHCH <sub>2</sub> I  CH <sub>2</sub> =CHCH <sub>2</sub> CH(CN  Note: References 577-1080 are on pp. 322-331.  * The methyl ester was used in this experiment.	The constraints were added in inverse order. Then originally isolated this product was perione derivative indicated (ref. 712).

TABLE VI—Continued

Alkylation of Cyanoagetic Esters,  $\mathrm{CH_2(CN)CO_2R}$ (The ethyl ester was used unless otherwise specified.)

Refer-	couc	123		170		127	185	307	528			288, 40	871	973, 975	027	•	290 86	****	01	2	288	
	Solvent	CH,0H	Ether	Ethanol	CH <sub>2</sub> OH	Ethanol	Ethanol	Ethunol	Ethanol			Ethanol	Ethanol	Ethanol		Ethanol		Ethunol	110 11 %	1.0,11,011	Ethanol	
	Baso	Na0CH,	NuOC, FIS	NaOC,IIs	NaOCH,	Va OC 11.	No.0C,113	NaOC, II,	VaOC. II.	511		NaOC,II,	VaOC 11.	XaOC 11	STROOMS	NaOC, II,		NaOC,115		NaOCill, i cittly ou	Man of H	\$ 11800mx
201 14 1011	Yiold,	2	i	98	1	ę	5 8 8	2 1	Ę	5		92		3 6	;	-		#	1	Ξ	20	e e
(The ethyl ester was used uniess outer with the ethyl ester was a second to the ethyl ester was a second to the ethyl ester with the ethyl ester was a second to the ethyl ester was a secon		Product	CH, COCH, CH(CN)CO, CH;	CHICOCHICH(CN)COICEILE	[NG(CH <sub>2</sub> ) <sub>2</sub> ] <sub>2</sub> C(C <sub>1</sub> N/CO <sub>2</sub> C <sub>2</sub> 113 Ctr O CCH CH(CN)CO <sub>2</sub> CH <sub>1</sub> * and	(CH, O, CCII,), C(CN) CO, CII,	CI(CH,),CH(CN)CO,C,H,	Br(CH <sub>1</sub> ),CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> G H O CCH(CN)CH <sub>1</sub> ),CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> and	ethyl 1.cyanocyclobutane-1.carboxylate	H, CCHCH, CIICN	0;		n.C,H,CH(CN)CO,C,H,	$C_{1}II_{3}O(CII_{4})_{2}CH(CN)CO_{2}C_{2}II_{2}$	C II CHICKICO CIII	CH CH(CN)CO'C'II. and	CONTRACTOR OF THE PROPERTY OF	(; C.H. CH(CN)CO,C,H;	(i.c.it.),c(cN)co,c,it.	CALCIN CHICKNOO, II	((:C413)2C(CN)CO2C4H3-i§	$C_2H_sCH(CH_1)CH(CN)CO_2C_2H_s$
		Alkylating Agent	CH,COCH,CI	CH,COCH,CI	NC(CH2),OSO,C,H,CH3.P	CICH,CO,CH,	Cl(CH,),Br	Br(CH1,)3Br	$\mathrm{Br}(\mathrm{CH_2})_{\mathfrak{I}}\mathrm{Br}$	H,CCHCH,		$C_{\bullet}$	a.C.H.Br	CH O/CH.).Br	C2113 C ( C1127/201	i-C,H,Br	i.C.H.Br	•	i.C,H,I		$i.C_iH_pI$	$C_2H_5CH(CH_1)Br$

			T	HE	AL	KY.	LA	TI	ON	O)	F	ES	TJ	ER	S	A	ND	N	IT	$\mathbf{R}\mathbf{I}$	$\mathbf{L}$	ES		26
976	498, 497	528		201				731, 974,	977	* 0.0		185	127	127, 238	973, 978	200		39		470	167 074	970		
Ethanol CIL (CANO) CIL CIL	Cfl <sub>2</sub> (CN)CO <sub>2</sub> C <sub>2</sub> Fl <sub>5</sub> -C <sub>6</sub> H <sub>6</sub> Ethanol	Ethanol		Ethanol				Ethanol	Tehonol			Ethanol	Ethanol	Ethanol	Ethanol	Ethanol		i-C <sub>5</sub> H <sub>11</sub> OH		Ethanol	Ethanol	Ethanol		
NaOC2H5	NaOC,H,	NaOC <sub>2</sub> H <sub>5</sub>		$NnOC_2H_5$				$NaOC_2H_5$	NoOr H	2005		NaOC2H5	$NaOC_2H_5$	$\mathrm{NnOC_2H_5}$	NaOC2H5	NaOC,H,	3	NaOC, H11-7 J.C, H11OH		$NaOC_2H_5$	NaOC,H,	NaOC,H,		
8	, e	83		40				1				82	63	63	92	}	28	}		45	70	100		
CH <sub>2</sub> CH=CHCH <sub>2</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>6</sub>	(CH3)2N(CH2)2CH(CN)CQ2C2H3 Ethyl 4-evanotetrahydropyran-4-carboxylate	(CH <sub>3</sub> ),CCH <sub>2</sub> CHCN	000	Ethyl 1.cyano-2-vinylcyclopropane.	1-earboxylate, ethyl 2-immo-3-cyano- 4-vinyleyelopentane-1-earboxylate and othyl	2-imino-3-cyano-5-vinylcyclopentane-	1-carboxylato	C2H & O2CCH2CH(GN)CO2C2H &	H.O.GOWDJO-HOWDOWDO.H.O	S1+E) e) ) / (1) ) )	1	n-C,H <sub>11</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	n.C.H.,CH(CH3)CH(CN)CO2C2H5	(U,H,s),CHCH(CN)CO,C,H,s	$i \cdot C_5 H_{11} CH(CN) CO_2 C_2 H_3$	$(i \cdot C_sH_{11}CH(CN)CO_2C_2H_s)$	((i-C,H <sub>11</sub> ) <sub>2</sub> C(CN)CO,C <sub>2</sub> H,	(i-C <sub>5</sub> H <sub>11</sub> CH(CN)CO <sub>2</sub> C <sub>5</sub> H <sub>11-i</sub>    and	((*-C <sub>5</sub> H <sub>11</sub> ) <sub>2</sub> C(CN)CO <sub>2</sub> C <sub>5</sub> H <sub>11</sub> -;	Control (Cha)CH(CN)CO2C2H,	C2H5U2CCH(CH3)CH(CN)CO2C2H5	$[C_2H_5O_2C(CH_2)_2]_2C(CN)CO_2C_2H_5$	* The methyl ester was used in this experiment.  § The isobutyl ester was used in this experiment.	contained some of the othyl ester.
CH3CH=CHCH2Br	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl Cl(CH <sub>2</sub> ),O(CH <sub>2</sub> ),Cl	$(CH_3)_2$ C—— $CH_2$	<u>&gt;</u>	$BrCH_2CH = CHCH_2Br$				COM COLCAN	Cl3CCO,C,H,	Q	in the case of the	"Cultural	C U CITE	Colls/20mbr		i.C,H,,I	:	$i\text{-}\mathrm{C}_{5}\mathrm{H}_{11}\mathrm{I}$	¿·C.H.CH/CH ve.	CH,CHB,CO F	TOH VOO A II	1(0112)2(02(2H 5	Note: References 577-1 * The methyl ester was § The isobutyl ester was	The product also cont

## TABLE VI-Continued

Alkylation of Cyanoacetic Esters,  $\mathrm{CH_2(CN)CO_2R}$  (The ethyl ester was used unless otherwise specified.)

Pofor.	oneo	273	469 127 470 460 130 980 167, 981 185, 982 469 89 150, 322 528 325 325	89 469 128
	ent	lor	Ethanol Ethanol Ethanol Ethanol Stilanol Ethanol	None Ethanol Ethanol
	Solvent	Ether	Ethan Ethan Ethan Ethan CH <sub>1</sub> (C Ethan Ethan Ethan Nono  — Ethan Ethan	None Ethan Ethar
•	Baso	Na	NaOC,H,	K2CO3 NaOC2H6 NaOC2H5
	Yield, %	29	70 50 60 60 60 63 62 62 74 70 17	84 70 71
(The ethyl ester was used ancest concernation)	Product	C(CN)CO <sub>1</sub> C <sub>2</sub> H <sub>3</sub> C <sub>1</sub> H <sub>2</sub> O <sub>2</sub> C(NC)C——C(CN)CO <sub>1</sub> C <sub>2</sub> H <sub>3</sub>	n.C <sub>6</sub> II <sub>13</sub> CJI(CN)CO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> n.C <sub>1</sub> II <sub>5</sub> CJI(CH <sub>3</sub> )CH(CN)CO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> i.C <sub>1</sub> II <sub>5</sub> CII(CH <sub>3</sub> )CH(CN)CO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> (C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> CHCII <sub>4</sub> CH(CN)CO <sub>5</sub> C <sub>4</sub> H <sub>5</sub> (C <sub>2</sub> II <sub>5</sub> ) <sub>2</sub> CIC(II <sub>5</sub> ) <sub>2</sub> CII(CN)CO <sub>5</sub> C <sub>4</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> O <sub>5</sub> CCII(C <sub>2</sub> H <sub>5</sub> )CH(CN)CO <sub>5</sub> C <sub>4</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> O <sub>5</sub> CCII(C <sub>2</sub> H <sub>5</sub> )CH(CN)CO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> O <sub>5</sub> CCII(C <sub>4</sub> ) <sub>3</sub> CH(CN)CO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> C <sub>4</sub> H <sub>5</sub> O <sub>5</sub> CCII(C <sub>4</sub> ) <sub>3</sub> CH(CN)CO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> C <sub>4</sub> H <sub>5</sub> O <sub>5</sub> CCII(C <sub>4</sub> ) <sub>3</sub> CH(CN)CO <sub>5</sub> C <sub>5</sub> H <sub>5</sub> Ethyl cyclohaxylandonanic acid (Ethyl dyclohaxylandonanic acid (Ethyl di-(2-cyclohaxenylcyanoacetato (Ethyl di-(2-cyclohaxenylcyanoacetato Bthyl (2,4-dinitrophenyl)cyanoacetate Ethyl (2,4-dinitrophenyl)cyanoacetate	n.C,H13CH(CO2H)2 n.C,H13CH(CN)CO2C2H5 n.C,H11CH(CH3)CH(CN)CO2C2H2
	Affections Acoust	BrCH(CN)CO <sub>3</sub> C <sub>3</sub> H <sub>3</sub>	C <sub>4</sub> n.C <sub>4</sub> H <sub>13</sub> Br  n.C <sub>4</sub> H <sub>5</sub> CH(CH <sub>5</sub> )Br  i.C <sub>4</sub> H <sub>5</sub> CH(CH <sub>5</sub> )Br  (C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub> CHCH <sub>4</sub> Br  (C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub> CHCH <sub>4</sub> Br  (C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub> CHCH <sub>4</sub> Br  (C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub> CHCH <sub>5</sub> Br  (C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub> CHCO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> (CH <sub>5</sub> ) <sub>2</sub> CBrCO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> (CH <sub>5</sub> ) <sub>2</sub> CBrCO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> (CH <sub>5</sub> ) <sub>2</sub> CBrCO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> (CH <sub>5</sub> ) <sub>2</sub> CBrCO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> (CH <sub>5</sub> ) <sub>2</sub> CBrCO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> (CH <sub>5</sub> ) <sub>2</sub> CBrCO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> (Cyclohexyl bromide Cyclohexyl iodide Cyclohexyl iodide Cyclohexyl iodide Cyclohexyl iodide Cyclohexyl iodide Cyclohexyl iodide H <sub>5</sub> -Dihromocyclohexano Cyclohexyl iodide PrO <sub>5</sub> NC <sub>6</sub> H <sub>5</sub> Cl  2,4-Dinitrochlorobenzeno Prieryl chlorido	C, n.C,H <sub>13</sub> Br n.C,H <sub>13</sub> Br n.C,H <sub>13</sub> Br

					,	ГН	E	A.	LK	(Y)	LA	TI	10	₹ (	ЭF	E	ST	Έl	RS	A	N	0 1	Νľ	TR	IL	ES			
984	283	982	185	629		984	721	470	470	470	470	95		83	83		38		116.95	569	198	112	!	686	1		469	80	170
Ethanol	1	Ethanol	Ethanol	Ethanol		Ethanol	Nono	Ethanol	Ethanol	Ethanol	Ethanol	None		$(n-C_3H,0)_2$ CHCH3	(n.C,H,O)CHCH,		сноно		Ethanol	Ethanol	Ethanol	Ethanol		Ethanol		,	Ethanol	Ethanol	
$NaOC_2H_5$	}	$NaOC_2H_5$	NaOC2H5	$NaOC_2H_{\delta}$		NaOC <sub>2</sub> H <sub>5</sub>	Na	$NaOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub>	NaOC2H5	NaOC2H5	Na		КОН	KOH		NaOCH3		NaOC,H,	NaOC.H.	NaOC, H.	NaOC2H5		NaOC,H,	1	TI DOM	NaOC2H3	NaOC, H.	3
44-50	I	30	85	83		44-50	58	51	18	33	33	ļ		40	30	14	Poor	Poor	09	Good	42	1		44		E E	2 %	63	
$C_2H_5O_2CCH(C_3H_7\cdot n)CH(CN)CO_2C_2H_5$	C2H5O2C(CH2)2CH(CH3)CH(CN)CO2C2H3	C2H5O2C(CH2)4CH(CN)CO2C2H5	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ),CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	Dicthyl 1-cyanocyclopentane-	1,2-dicarboxylate	C2H5O2CCH(C3H7-i)CH(CN)CO2C2H5	C2H5O2CCH(CH2OC2H5)CH(CN)CO2C2H5	Ethyl (cyclohexylmethyl)cyanoacctate	Ethyl (2-methylcyclohexyl)cyanoacetato	Ethyl (3-methylcyclohexyl)cynnoacetate	Ethyl (4-methylcyclohexyl)cyanoacctate	C.H.CH.CH(CN)CO.C.H. and	$(C_4H_5CH_2)_2C(CN)CO_2C_2H_5$	C,H,CH,CH(CN)CO,C,H,	$\{C_6H_5CH_2CH(CN)CO_2C_2H_5\}$	(C,H,CH2)2C(CN)CO2C2H,	$\{C_6H_5CH_2CH(CN)CO_2H\}$	((C,H5CH2)2C(CN)CO2CH3*	C,H,CH,CH(CN)CO,C,H,	$(C_4H_5CH_2)_2C(CN)CO_2C_2H_5$	o-CIC,H,CH,CH(CN)CO,C,H,	0.02NC,H4CH2CH(CN)CO2C2H5 and	(0-02NC6H4CH2)2C(CN)CO2C2H5	C,H,GH,CH(CN)CO,C,H,		n-C,H,,CH(CN)CO,C,H.	$n$ -C $_{\circ}^{\circ}$ H $_{1}$ ,CH(CO $_{\circ}$ H),	n-C,H13CH(CH3)CH(CN)CO2C2H5	000 000 22 000 001
n-C <sub>3</sub> H,CHBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	CH3CHBr(CH2)2CO2C2H5	$\mathrm{Br}(\mathrm{CH}_2)_1\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5$	$I(CH_2)_4CO_2C_2H_5$	$\mathrm{Br}(\mathrm{CH_2})_3\mathrm{CHBrCO}_2\mathrm{C}_2\mathrm{H}_5$		$i$ -C <sub>3</sub> H,CHBrCO <sub>2</sub> C <sub>2</sub> H $_s$	C2H,OCH2CHBrCO2C2H,	Cyclohexylmethyl iedide	2-Mothyleyelehexyl bromide	3-Methyleyelohexyl bromide	4.Mcthylcyclohexyl bromide	$C_0H_3CH_2CI$		$C_{i}H_{i}CH_{i}CI$	C,H,CH,Cl	2	C,H,CH,CI		CLH 5CH 2CI	C6H5CH2CI	o-CIC,H,CH,CI	O·O2NC6H4CH2CI		Cenech2br	$C_{\mathrm{s}}$	$n$ - $C_8H_1$ Br	$n ext{-}\mathrm{C}_{8}\mathrm{H}_{17}\mathrm{I}$	$n$ -C $_6$ H $_1$ 3CH(CH $_3$ )Br	Note: References 577-1080 are on zz. 220 223

Note: References 577-1080 are on pp. 322-331, \* The methyl ester was used in this experiment.

## TABLE VI-Continued

# ALKYLATION OF CYANOAGETIC ESPERS, CH<sub>2</sub>(CN)CO<sub>2</sub>R (The othyl ester was used unless otherwise specified.)

	Tho othy total transparent				Rofer-
		Yiold,	Baso	Solvent	onco
4	Product	0	į		469
Alkylating Agent	H O OOMOAND MAY IN THE THE	20	$\mathrm{NnOC_2H_6}$	Ethanol	i C
$n.C,H,CII(C_2H_5)CH_2Br$	n-C,H,CH(C2Hs)CH2CH(CM)CC2C2+18	81	$NaOC_2H_5$	Ethanol	007
%.C.H.,CH(CH,)I	¿.C,H13CH(CH3)CH(CN)CO2C2TIS	12	NaOC,H,	Ethanol	989
TO HE CHERCO, C. H.	C,H,O,CCH(C,H,-i)CH(CN)CU,C,Hs	ò	NoOC.H.	Ethanol	629
P-/CHUNCHUNCHUNCHUNCHUNCHUNCHUNCHUNCHUNCHUN	Diethyl 2-cyano-1-methylcyclopentane-	l	74000		
Dr(C112/3/Dr(C113/002-2-5	1,2-dicarboxylato		11 000 11	Ethanol	974
11 0 00 0000	mistry organotricarballylato	١	NaOC2113		753
C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> CHBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	TITOURY & C. T 9 00000000000000000000000000000	1	NaOCH3	CH3On	
CH3O,CCHBr(CH2),CHBr.	Trimetnyi 2-cymiocy occursoriato*				
CO,CH,	pentane-1,2,3-tricurnes,4400				
(low-molting form)			NaOCH.	CH,OH	753
CH.O.CCHBr(CH.),CHBr.	Trimethyl 2-cyanocyclo-	1		•	
CO.CH.	pentanc-1,2,3-triearboxylato*				
0020113	•				175
(high-molting form)		1	$NaOC_2H_b$	Ethanol	21.1
C,H,O,CCHBrCHBr-	Trictnyl Leyanocyclo-				
COCH	propane-1,2,3-tricarboxylato				
(meso form)		ì	H DOW	Ethanol	175
CITE CONTROL	Thistbut 1 organoryclo.	30	NEO COLLS	TOURING	
C2H,O2CCHBrCHBr-	Titeonyt And micely on				
$\mathrm{CO_2C_2H_5}$	propulation, 2, 0 to the contract of the contr				
(+, - form)		40	Manc. H.	Ethanol	127
A Casabbayalothy I bromide	Ethyl ( $\theta$ -evelolioxylethyl)eyanoneetato	2	TAROOTTS		460
p-cyclottexyteenty in crimes	THE CHICANOL C. H.	78	NaOC,H	Ethanol	201
$C_6H_5(CH_2)_2Br$	Cons(OII2)2OII(OII)CO2C2FES	١	NaOC,H,	Ethanol	105
$C_{\mathbf{k}}H_{\mathbf{k}}(CH_{\mathbf{s}})_{\mathbf{k}}Br$	[C <sub>6</sub> H <sub>6</sub> (CH <sub>2</sub> ) <sub>2</sub> ] <sub>2</sub> C(CN)OO <sub>2</sub> C <sub>2</sub> 11 <sub>5</sub>	00	H DOW	Ethanol	185
	$(C_sH_sO(CH_s)_sCH(CN)CO_sC_sH_s$	70	244002445		
$C_bH_sO(CH_2)_2Br$	(rc, H, O(CH,), 1, C(CN)CO, C, H,	35			198
- C / 110/0 11 0:00	COLUMN CHICKNOO CHE	25	NaOC,H.	Ethanol	021
p-ClC <sub>6</sub> H <sub>4</sub> U(CH <sub>2</sub> ) <sub>2</sub> Br	p-0.00 61140 (0112)201100 010-0				

																	-							
470	470	470	983	123		123, 124	100	193	861	198, 111	185		127	176		469	985	121	127	198	886	02 <del>+</del>	128	127
Ethanol	Ethanol	Ethanol	Ethanol	СН3ОН		Ethanol	Ethanol	1	Ethanol	Ethanol	Ethanol-ether		Ethanol	Ethanol	,	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol
NaOC,H,	NaOC <sub>2</sub> H <sub>5</sub>	NaOC, H5	NaOC, H5	$NaOCH_3$		NaOC, H,	NaOC, II,	· '	NaOC, H,	NnOC2H3	NaOC <sub>2</sub> H <sub>5</sub>		NaOC,H,	NaOC,H,	H JUCK	211200113	NaUC <sub>2</sub> H s	$NnOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub>	$NaOC_2H_5$	NaOC <sub>2</sub> H <sub>5</sub>	NaOC,H,	NaOC,H.	NaOC <sub>2</sub> H <sub>5</sub>
55	55	<del>\$</del>	48	1		1	ł	ł	Good	80	95		70	20	ď	3 ;	)  -	45	38	65	G <del>†</del>	50	2 8	92
o-CH3C6H4CH2CH(CN)CO2C2H5	m-CH3C6H4CH2CH(CN)CO2C3H3	p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub>	p-CH3OC,H4CH2CH(CN)CO2C2H3	C,H,COCH,CH(CN)CO,CII,* and	Cold Court (Cold Cold Cold Cold Cold Cold Cold Cold	Conscionation (CN)CO.C.H.	(C,H,COCH,)2C(CN)CO,C,H,	C.H.COCH2CH(CN)CO2C3H2-n¶	o-NCC,H,CH,CH(CN)CO,C,H;	(o·NCC,H,CH,)2C(CN)CO2C2Hs	C(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	4	n-C <sub>9</sub> H <sub>19</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>x</sub> Triothyl 9	1.2.3-trienthoxylete	$C_6H_5(CH_2)_3CH(CN)CO_2C_2H_5$	C,H,O(CH,),CH(CN)CO,C,H	o-BrC,H,O/CH,),CVZCZZZZ	2.4.Cl.C.H.O.CH.O.CH.C.L.C.	a-Bro H Older ) Striction Contraction	C.H.CH.S.CH > CH.CN.SO A II	p-C,H,C,H,CH,CH,CN,CO,C,H,	p-CH <sub>3</sub> C <sub>6</sub> H <sub>2</sub> O(CH <sub>3</sub> ), CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub>	Ethyl I-indanylevanoacetate	Note: References 577-1080 are on pp. 322-331.
o-CH3C6H4CH2Br	m-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Br	P-CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CI	P-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CI	Censcoch2Br	"מ אינו אינו	Offit SCOOTING	Conscionation of the contract	Constant of the constant of th	S-NCC, H, CH, CI	CTOO ENTON	CH <sub>2</sub> Br	O,	$n$ -C, $H_{19}$ Br C, $H_5$ O,CCHBrCH	CHBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>3</sub> Br	OensO(CH2)3Br	$o ext{-BrC}_6 ext{H}_4 ext{O}( ext{CH}_2)_3 ext{Br}$	$2$ ,4-Cl <sub>2</sub> C $_6$ H $_3$ O(CH $_2$ ) $_3$ Br	$p ext{-BrC}_6 ext{H}_1 ext{O}( ext{CH}_3),  ext{Br}$	C6H5CH2S(CH2)2CI-KI	$p ext{-}\mathrm{C}_2\mathrm{H}_5\mathrm{C}_6\mathrm{H}_4\mathrm{CH}_3\mathrm{C}$	p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> O(CH <sub>2</sub> ) <sub>2</sub> Cl	1-Bromoindane	Note: References 577-1

 $\P$  The *n*-propyl ester was used in this experiment. \* The methyl ester was used in this experiment.

Refer-

## TABLE VI—Continued

Alkylation of Cyanoacetic Esters,  $\mathrm{CH_2(CN)CO_2R}$  (The ethyl ester was used unless otherwise specified.)

20000	986	986	469 787	471 128 128 150	986	
	Solvent	1 1	Ethanol Ethanol	Ethanol Ethanol Ethanol	1	
	Вазо	1 1	NaOC2H5 NaOC2H5	NaOC,H, NaOC,H, NaOC,H,	I	
Yield,	%	1 1	65 55	57 44 60	1	
	Produc $t$	Ethyl chloroindenonylcyanoacotato** Ethyl bromoindenonylcyanoacetate** and diothyl indenone-2,3-dieyanoacetate	n-C <sub>1,0</sub> H <sub>21</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> C-H-O-C(CH <sub>5</sub> ),CH(CO <sub>3</sub> C <sub>2</sub> H <sub>5</sub> )-	CH(CN)CO1C.Hs [m.CH,C,H,O(CH,S),1,C(CN)CO1C,Hs p.CH,C,H,O(CH,S),2CH(CN)CO1C,Hs p.CH,C,H,O(CH,S),CH(CN)CO1C,Hs p.C2H,C,H,O(CH,S),CH(CN)CO1C,Hs	CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> and	CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub>
	4000	Alkylating Agene 2,3.Dichloroindenone 2,3.Dibromoindenone	G10 n.C10H21Br	C2H3OCHBICOLING CO2C3H3 m-CH2C4H4O(CH2)3Br p-CH3C4H4O(CH2)3Br p-C2H5C6H4O(CH2)3Br	5 0={ «	5 5 0

$n\text{-}C_{11}H_{22}I$ $m\text{-}C_2H_5C_6H_4O(\text{CH}_2)_3\text{Br}$ $p\text{-}C_2H_5C_6H_4O(\text{CH}_2)_3\text{Br}$ I-Chloromethylnaphthaleno	n-C <sub>11</sub> H <sub>13</sub> CH(CO <sub>2</sub> H) <sub>2</sub> [m-C <sub>2</sub> H <sub>5</sub> C <sub>6</sub> H <sub>1</sub> O(CH <sub>2</sub> ) <sub>3</sub> ] <sub>2</sub> C(CN)CO <sub>2</sub> C <sub>2</sub> II <sub>5</sub> p-C <sub>2</sub> H <sub>5</sub> C <sub>6</sub> II <sub>1</sub> O(CH <sub>2</sub> ) <sub>3</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> Ethyl (1-naphthylmothyl)cyanoacetate	81 40 70 45	K,CO, NnOC,H; NnOC,H; NnOC,H;	None Ethanol Ethanol	89 471 128 469
$C_{12}$ $n$ - $C_{12}\mathrm{H}_{25}\mathrm{Br}$	n-C <sub>12</sub> H <sub>25</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	55	NaOC, H, Ethanol	Ethanol	138
C <sub>10</sub> -C <sub>13</sub> n-C <sub>16</sub> H <sub>33</sub> I n-C <sub>16</sub> H <sub>33</sub> Br (C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> CBr	n-C <sub>16</sub> H <sub>33</sub> CH(CO <sub>2</sub> H) <sub>2</sub> n-C <sub>16</sub> H <sub>33</sub> CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> (C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> CCH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	90 75 Poor	K,CO, NaOC,II; NaOC,II;	None Ethanol Ethanol	89 721 586
Note: Reference 577_1090 and on 1999	000 000 000 000				

C.

Note: References 577-1080 are on pp. 322-331.

\*\* The structure of the product was not determined.

†† The position of the double bond was not stated.

#### TABLE VII

Alkylation of Bromo., Acetamido., and Phenylacetamido.cyanoacetic Esters,  $\mathrm{XCH}(\mathrm{CN})\mathrm{CO}_2\mathrm{R}$ (The ethyl ester was used unless otherwise indicated.)

		The ethyl ester was used unless collect may				
			Yield,			Refer-
		tool	%	Base	Solvent	onco
×	Alkylating Agent	Produce	26	Aniline	Ethor	273
ž.	None	Triethyl 1,2,3-tricyanocyclopropane-	ì			
ā		1,2,3-tricarboxylato rejethyl 1,2,3-tricyanocyclopropane-	00	Na	Ether	273
	None	1.9.3-trienrboxylato			13410011	626
	*	OF CONHECON VCNICO, C. H.	71	NaOC, H	Ethanor	7 6
CH, CONH	$CH_3I$	Series Control of the	855	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	232
	$\mathrm{C_2H_5Br}$	CH3CONIC(C2H2)(CR)C2C2H3	20	NaOC,H,	Ethanol	232
	n-C <sub>3</sub> H,Br	CH <sub>3</sub> CONIIC(C <sub>3</sub> H <sub>3</sub> ·n)(CN)CO <sub>2</sub> C <sub>2</sub> II <sub>3</sub>	9	NaOC, II,	Ethanol	241
	$CH_3S(CH_2)_2CI$	CH <sub>3</sub> S(CH <sub>2</sub> ) <sub>2</sub> C(NHCCCH <sub>3</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub>	99	NaOC, II,	Ethanol	241
	$i.\mathrm{C}_3\mathrm{H},\mathrm{Br}$	CH <sub>3</sub> CONHC(C <sub>3</sub> H <sub>3</sub> -1)(CIN)CO <sub>2</sub> C <sub>2</sub> 116	6	NAOC, H.	Ethanol	232
	CH2=CHCH2Br	CH <sub>3</sub> CONFIC(CH <sub>2</sub> CH=CH <sub>2</sub> )(CM/CO <sub>2</sub> C <sub>2</sub> L <sub>2</sub> S	0 0	ZOUZ.	Ethanol	232
	n-C,H,I	CH <sub>3</sub> CONHC(C <sub>4</sub> H <sub>9</sub> ·n)(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	2 2	Moor H.	Ethanol	241, 232
	A.C.H.Br	CH,CONHC(C,H,;)(CN)CO2C2H5	3	11000115	Tatl	999
	CITY DOUBLE OF THE CI	CH CONHCICH, CICH, )-CH, 1(CN)CO, C, H,	65 80	NaOC, H5	Ethanol	15. 15.
	CH <sub>2</sub> =C(CH <sub>3</sub> )CH <sub>2</sub> Ci	Ethyl $\alpha$ -acetamido- $\alpha$ -eyano- $\beta$ -	99	$NaOC_2H_5$	Ethanol	14.5
	methylimidazole	(4-imidazolyl)propionato				
	hydrochlorido		ļ		1341.00.01	699
	n-C,H,Br	$\mathrm{CH_3CONHC}(\mathrm{C_5H_{11}}.n)(\mathrm{CN})\mathrm{CO_2C_2H_5}$	57	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	1 000
	n-0:H:-I	$_{\mathrm{CH,CONHC}(\mathrm{C,H_{i,a}},n)}(\mathrm{CN})\mathrm{CO_{2}\mathrm{C}_{2}\mathrm{H}_{3}}$	81	NaOC2H5	Ethanoi	232
	"Curily"	CH CONFICICIHn)(CN)CO,C,H,	65	$NaOC_2H_5$	Ethanol	535
	2 11 21 21 C	OH CONHECT HE HANGNICO TO	83	$NuOC_2H_5$	Ethunol	241
	Censchiol	OHIOONHOOMEN WONNOON H.	81	NaOC,H,	Ethanol	232
	n-C <sub>8</sub> H <sub>17</sub> I	Chacolatic(Carifolic)(Carifolic)	96	NAOC,H.	Ethanol	2.42
	p-CH <sub>3</sub> OC <sub>4</sub> H <sub>4</sub> CH <sub>2</sub> Br	p-CH <sub>2</sub> CC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(MHCCCH <sub>3</sub> NCM)CC <sub>2</sub> C <sub>2</sub> H <sub>3</sub>	33 6	NaOC2H5	Ethanol	232
	$n \cdot C_9 H_{19} Br$	CD30CD110(081107/01/10/10/01/10/01/10/01/10/01/10/01/10/01/10/01/10/01/10/01/10/01/10/01/10/01/10/01/10/01/10/01/01				

242	242	243	243	243	244	243	244	243	245		245	i	945	, i	2,0	Ç.	276	0.50
Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	$CH_3OH$	Ethanol	$CH_3OH$	Ethanol	Ethanol		C.H.	3	Ethanol	TOURING	Dehonol	Enitation	Tithonol	Elianoi
$NaOC_2H_5$	NaOC2H5	NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub>	NaOC,H,	NaOCH,	NaOC <sub>2</sub> H <sub>5</sub>	NaOCH <sub>3</sub>	NaOC,H	NaOC,H,		Ŋa		NaOC.H.	\$ (2)	Man d	214002115	Man H	MacCons
75	80	ca. 76	Į	[	ĺ	Į	ĺ	Į	20		Door	4	80	<b>)</b>	020	3	20	2
C <sub>8</sub> H <sub>4</sub> O <sub>2</sub> N(CH <sub>2</sub> ) <sub>3</sub> C(NHCOCH <sub>3</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> *	$G_8H_4O_2N(CH_2)_1C(NHCOCH_3)(CN)CO_2C_2H_5^*$	CH <sub>2</sub> S(CH <sub>2</sub> ),C(C <sub>8</sub> H <sub>8</sub> ON)(CN)CO <sub>2</sub> CH <sub>3</sub> †	¿-C3H,C(C8H8ON)(CN)CO2CH3†	¿-C,H,C(C,H,ON)(CN)CO2CH,†	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C(C <sub>6</sub> H <sub>6</sub> ON)(CN)CO <sub>2</sub> CH <sub>3</sub> †	C,H3CH2C(C,H6ON)(CN)CO2CH3	p-CH3OC,H4CH2C(C,H9ON)(CN)CO2CH3	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> C(C <sub>6</sub> H <sub>6</sub> ON)(CN)CO <sub>2</sub> CH <sub>3</sub> †	$p ext{-} ext{CH}_3 ext{C}_6 ext{H}_1 ext{SO}_2 ext{C}_6 ext{H}_4 ext{CH}_2 ext{-}$	C(C,H,ON)(CN)CO,CH,†	p-CH3OC,H,SO,C,H,CH2.	C(C,H,ON)(CN)CO,CH,†	p-CH3OC,H3O2C,H,CH3.	C(C,H,ON)(CN)CO,CH,†	O.S[C,H,CH,C(C,H,ON)(CN)CO,CH,,n].+		p-CH,00c,H,00C,H,CH,.	C(C,H,ON)(CN)CO,CH,†
$\gamma ext{-Phthalimidopropyl}$	bromide 8-Phthalimidobutyl iodide	CH <sub>3</sub> S(CH <sub>2</sub> ) <sub>2</sub> Cl	i.C3H,1	:-C4H,I	C,H,CH,CI	C,H,CH,CI	$p$ -CH $_3$ OC $_6$ H $_4$ CH $_2$ CI	p-CH3OC,H4CH2Cl	$p ext{-}\mathrm{CH}_3\mathrm{C}_8\mathrm{H}_4\mathrm{SO}_2 ext{-}$	$\mathrm{C_8H_4CH_2Br}{ extstyle -p}$	p-CH <sub>3</sub> OC <sub>8</sub> H <sub>4</sub> SO <sub>2</sub> -	$\mathrm{C_6H_4CH_2Br}{ extstyle F}$	$p$ -CH $_3$ OC $_8$ H $_4$ SO $_2$ -	$\mathrm{C_{e}H_{2}CH_{2}Br}$	$p ext{-BrCH}_2\mathbf{C}_0\mathbf{H}_4\mathbf{SO}_2$ -	$\mathrm{C_{s}H_{2}CH_{2}Br}{p}$	p-CH3OC,H3COC,H3-	$\mathrm{CH}_2\mathrm{Br}.p$
		ONH (NO)																

\* The ethyl acetamidocyanoacetate used contained radioactive carbon. † The methyl ester was used in this experiment.

#### TABLE VIII

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Alexelation of Monoalexelcyanoacetic Esters, RCH(CN)CO<sub>2</sub>R'

			`	J11 (3214	110 1113				
Bofor.	eneo	988	989, 164	145	562 971, 972	239 240 252	575 44, 51, 227	975 214 575 976	974 980, 974 974
	Solvent	Ethonol	Ethanol	Ethanol	Ethanol Ethanol	Ethanol Ethanol Ethanol	NaOC <sub>2</sub> H <sub>3</sub> Ethanol NaOC <sub>3</sub> H <sub>7</sub> -n (n.C <sub>3</sub> H <sub>7</sub> O) <sub>3</sub> CO	Ethanol Ethanol Ethanol	CH,OH Ethanol Ethanol
ated.)	Base	NaOC <sub>2</sub> H <sub>5</sub>	$Na0C_2H_5$	$NnOC_2H_5$	NnOC,H; NnOC,H;	NaOC,H, NaOC,H, NaOC,H,	NaOC,H, NaOC,H,-n	NaOC2Hs NaOC2Hs NaOC2Hs NaOC2Hs	NaOCH, NaOC2H, NaOC2H,
o indic	Yield, %	l	ca. 100	20	1 88	86 76 95	87 78	1 55 05	15
ALEXYLATION OF MUNICALES. ALEXALIS otherwise indicated.)	Product	C.H.O.CC(CH.)(CN)CH.	C(CH <sub>1</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CC(CH <sub>3</sub> )(CN)- CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub>	;.C3H,C(C2H5)(CN)CO2C2H5	$n.C_3H,C(C_2H_3)(CN)CO_3C_3H_6$ $CH_3=CHCH_2C(C_3H,\cdot n)(CN)$ -	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> i.C <sub>3</sub> H <sub>7</sub> C(C <sub>4</sub> H <sub>5</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> i.C <sub>3</sub> H <sub>7</sub> C(C <sub>4</sub> H <sub>7</sub> n)(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> (i.C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> C(CN)CO <sub>2</sub> C <sub>4</sub> H <sub>5</sub>	n.C,H,C(C,H,-i)(CN)CO,C,H, i.C,H,C(C,H,)(CN)CO,C,H,-n*	(i.C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> C(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> sec.C <sub>4</sub> H <sub>3</sub> C(C <sub>3</sub> H <sub>7</sub> ·n)(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> (sec.C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> C(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> ·	C(CH <sub>2</sub> CH=CH <sub>3</sub> )(CN)CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub> CH <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> C(CH <sub>3</sub> )(CN)CO <sub>2</sub> CH <sub>3</sub> † C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>2</sub> H <sub>5</sub> )(CN)CO <sub>2</sub> CH <sub>5</sub> C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> -n)(CN)- C <sub>3</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>3</sub> H <sub>7</sub> -n)(CN)-
Alkylation (The	Alkylating Agent		CH2 <sup>12</sup> (CH3) <sub>2</sub> CBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	i.C,H,I	C,H,I	C,H,I n-C,H,Br i-C,H,1	$i.\mathrm{C_3H},\mathrm{Br}$ $\mathrm{C_2H_5Br}$	; C, H, I n-C, H, Br sec-C, H, Br CH CHCH. Br	CH,I C,H,I n-C,H,I
	р	$C_1$	CH,	<i>0</i> 3 C.H.	$C_3$ $n$ · $C_3$ H $_7$	$i.\mathrm{C_3H_7}$	O., n-C.H., i-C.H.,	sec.C <sub>4</sub> H <sub>9</sub>	CH <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub> CP <sub>3</sub> O <sub>2</sub> CCH <sub>2</sub>

	CICH,CO,C,H,		1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	776	
	Chichbrougous	C2 H5 C2 CCH (CH3) C(CN) CC2 C2 H5	]	NaOC2H5	Ethanol	974	
	$C_0H_5CH_2CI$	CH,O,CCH,C(CH,C,H,)(CN).	1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	974	
		CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>					THE
>S< (=C₄H₃S)	CICH, CO, C, H,	C <sub>2</sub> H <sub>s</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>1</sub> H <sub>3</sub> S)(CN).	09	K2CO3	(CH <sub>3</sub> )2CO	88	ALK
٤	2-Cyelohexenyl bromido	Ethyl 2-thienyl-(2-eyelohexenyl).	67	$\mathrm{NaOC_2H_5}$	Ethanol	187	ZLATI(
$(C_2H_\delta)_2$ CH	$\mathrm{C_2H_5Br}$	(C2H5)2CHC(C2H5)(CN)CO2C2H5	Good	$N_{8}OC_{2}H_{5}$	Ethanol	238, 983	о ис
$C_2H_5O_2CCH_2C(=NH)$	ICH2CN	$\begin{array}{c} \text{NH} - \text{C} = \text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5 \\ \text{HN} = \text{C}_3 \end{array}$	J	NaOC2H5	Ethanol	000	F E
$\mathrm{CH_3CH}(\mathrm{CO_2C_2H_5})$	$_{ m I}$	$\text{C}_2 \text{H}_5 \text{O}_2 \text{CCH} (\text{CH}_3).$	75	NaOC,H.	Ethanol	187 981	STER
	$n$ - $C_3$ H,I	C(CH <sub>3</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> C,H <sub>2</sub> O <sub>3</sub> CCH(CH <sub>2</sub> ).	5	i v		100 (101	RS A
	, A	C(C <sub>3</sub> H <sub>7</sub> ·n)(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	18	NaOC2H 5	Ethanol	985	ND
Č	†\chi\-'-	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH(CH <sub>3</sub> ). C(C <sub>4</sub> H <sub>3</sub> -i)(CN)CO,C,H,	1	$NaOC_2H_5$	Ethanol	985	NI
$(\mathrm{CH_3})_1\mathrm{C}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)$	CH <sub>3</sub> I	C.H.O.CC/CH		;			TRIL
2. Cropohowan	, ,	C(CH <sub>3</sub> )(CN)CO <sub>2</sub> C <sub>3</sub> H <sub>5</sub>	l	$NaOC_2H_5$	Ethanol	186	ES
$(=C_6H_9)$	$CH_3I$	C,H,C(CH,)(CN)CO,C,H,	85	$NaOC_2H_5$	Ethanol	290	
Note: References 5	Note: References 577-1080 are on pp. 322-331.	2-331.					

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\* The n-propyl ester was used in this experiment, † The mothyl ester was used in this experiment, † The halogen was not specified.

## TABLE VIII—Continued

Alexelation of Monoalexeloxanoacetic Esters, RCH(CN)CO<sub>2</sub>R' (The ethyl ester was used unless otherwise indicated.)

Refor-	enco	290, 991	290	290, 226	290	993	81	ć	88	001	201	001	502, 155	993	993	003		993	111	188		188	
	Solvent	Ethanol	Ethanol Tthanol	Ethanol	Ethanol	CH3CH(OC3H3-n); Ethanol	1.Butoxy.	2-ethoxyethane	CH3CH(OC, 11, -n);	Tolueno	Ethanol	Tolueno	Ethanol	Ethanol	Ethnool	-	Ethanol	Ethunol	•	Ethanoi Ether-toluene		Toluene	
	Baso	NaOC2Hs	NaOC,H,	NaOC,H.	NaOC,Hs	KOH	NaUC2115 KOH		кон	NaNH2	NaOC,H;	NaNH,	NnOC2H3	NaOC.H.	NaOC,Hs		NaOC,H5	NaOC,Hs		NaOC <sub>2</sub> H <sub>8</sub>	200	HNON	
	Yield, %	83-87	\$06	S (5	<u>6</u>	50	22	;	88	19	1	63	78	81	09	;	င်း	53		88	à	7	2
(The ethyl ester was used unless conc	,	Product	C,H,C(C,H,)(CN)CO,C,H, C,H,C(C,H,)(CN)CO,C,H,	C,H,C(C,H,-n)(CN)CO,C,H,	C(H,C(C,H,-n)(CN)CO2C2H3	$C_{s}H_{s}C(CH_{s}C_{s}H_{s})(CN)CO_{s}C_{s}H_{s}$	C,H,C(CH,)(CN)CO,C,H,	NCCH2C(CeH s)(CN)CC2C2118	NCCH C(C.H.)(CN)CO,C,H,	NCCH CC.H.)(CN)CO,C.H.	B.(CH.).C(C.H.)(CN)CO,C,H.	NOTE OF HOUSE OF HE	NO(CH,)2((Chris/Ch/)Ch/)Ch/	CI(CAL <sub>2</sub> ) <sub>3</sub> C(C <sub>6</sub> LL <sub>5</sub> )(CA)CC <sub>2</sub> C <sub>2</sub> 3	C.H.O.CCH,C(C.H.S)(CN)CO2C2775	C2H,U2CCA(CH3): C(C,H,)(CN)CO,C2H,	C <sub>2</sub> H <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> .	C(C,H <sub>5</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	$(\mathrm{CH_3})_2^{\mathrm{CBrCO}_2^{\mathrm{CzH_5}}}$ Constant $\mathrm{C(C_2^{\mathrm{H}_3})(CN)CO_2^{\mathrm{C}_2^{\mathrm{H}_3}}}$	C,H,CH,C(C,H,)(CN)CO,C,H,	C,H,CH,N(CH,)(CH,)2-	C(C,Hs)(CN)CO3C2Hs	C,H,CH,N(CH,NCH,N; C(C,H,N(CN)CO,C,H,
(The		Alkylating Agent	C <sub>2</sub> H <sub>5</sub> Br-KI	$C_2\Pi_5B^{\Gamma}$ $n$ - $C_3\Pi_7B^{\Gamma}$ - $KI$	n-C <sub>4</sub> H <sub>9</sub> Br-KI	n-C <sub>6</sub> H <sub>13</sub> Br-K1	CH <sub>3</sub> I	CICH,CN	***************************************	CICH, CN	CICH,CN	CH,BrCH,Br	CI(CH <sub>2</sub> ) <sub>2</sub> CN	$Cl(CH_2)_3Br$	CICH,CO2C2H3	CH,CHBrCO,C,H,	CI(CH2),CO2C2H5	11 000 000 000	(CH <sub>3</sub> ) <sub>2</sub> CBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	C,H,CH,CI	C,HSCH2N(CH3).	$(CH_2)_2Cl$	C,H,CH2N(CH3)- (CH2)3Cl
		R.	2-Cyclohexcnyl	$(==C_6H_9)$ (Cont.)			С.Н.	c ( , , p )															

$C_{r}$						
C2H5O2C(CH2)2CH(CH3) CH3I	$CH_3I$	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> CH(CH <sub>3</sub> )· C(CH <sub>3</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	1	$NaOC_2H_5$	Ethanol	283
n-C <sub>3</sub> H,CH(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> )	$n$ -C <sub>3</sub> H $_7$ I	$C_2H_5O_2CCH(C_3H_7-n)$ - $C(C_3H_7-n)(CN)CO_2C_2H_5$	78	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	984
$i \cdot C_3H_1CH(CO_2C_2H_5)$	$n\text{-}\mathrm{C_{3}H_{7}I}$	C2H5O2CCH(C3H7-1)- C(C3H7-1)(CN)CO2C2H5	83	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	984
	$i\text{-}\mathrm{C}_{3}\mathrm{H}_{7}\mathrm{I}$	C <sub>2</sub> H <sub>3</sub> O <sub>2</sub> CCH(C <sub>3</sub> H <sub>7</sub> ·i). C(C <sub>3</sub> H <sub>7</sub> ·i)(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	10	$NaOC_2H_5$	Ethanol	₹86
$C_sH_sCH_2$	$C_6H_5CH_2N(CH_3)$ - $(CH_3)_3CI$	C,H,CH,N(CH,)(CH,),- C(CH,C,H,)(CN)CO,C,H,	}	NaNH <sub>2</sub>	Tolueno	188
o-CH3C <sub>6</sub> H <sub>4</sub>	C,H,CH,N(CH,).	C,H,CH,N(CH,)(CH,),- C(CH,C,H,-0)(CN)CO,C,H,	65	NaNH2	Tolueno	188
$p ext{-} ext{CH}_3 ext{C}_6 ext{H}_4$	C,H,Br	p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> C(C <sub>2</sub> H <sub>5</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	09	NaOC <sub>2</sub> H <sub>5</sub>	$(C_2H_5O)_2CO$	44, 227
$i \cdot C_6H_{13}CH(CH_3)$	$C_2H_5O(CH_2)_2I$	C2H,0(CH2)2C(CN)CO2C2H5	80	X	Xyleno	750
i.C.H.CH(CO2C2Hs)	$i.\mathrm{C}_{i}\mathrm{H}_{i}\mathrm{Br}$	i-C,H1,CHCH, C,H,O,CCH(C,H,-i)-	1	NaOC,H,	Ethanol	985
C,H,COCH,	CH <sub>3</sub> I C <sub>2</sub> H <sub>3</sub> I	C,H,COCH,C(C,H,)CO,CCH,* C,H,COCH,C(C,H,)CN)CO,CH,* C,H,COCH,C(C,H,)CN)CO,CH,*	1 1	NaOCH <sub>3</sub> NaOC <sub>2</sub> H <sub>5</sub>	CH,OH Ethanol	123 123
ර්	Censon <sub>2</sub> OI	Corchic(CH <sub>2</sub> C,H <sub>5</sub> )(CN). CO <sub>2</sub> CH <sub>3</sub> *	1	NaOCH,	сн, он	123
l-Indanyl	$n ext{-}\mathrm{C}_3\mathrm{H}_7\mathrm{I}$	Ethyl 1-indanyl-(n-propyl)cyano- acetato	41	NaOC2H5	Ethanol	217
$(C_{\mathfrak{d}}H_{\mathfrak{z}})_{\mathfrak{z}}CH$	(C,H,),CHCI	$[(C_6H_5)_2CH]_2C(CN)CO_2C_2H_5$	1	BrMg	Ether	994
Note: References 577-1080 are on pp. 322-331.	-1080 are on pp. 322	-331.		enolate		

r was used in this experiment.

|| The bromomagnesium enolate was obtained by the addition of phenylmagnesium bromide to ethyl benzylidenecyanoaeetate.

#### TABLE IX

ALKYLATION OF ALKYLIDENEMALONONITRILES AND ALKYLIDENECYANOACETIC ESTERIS Yiold.

ALK	YLATION OF ALKYLID	ALKYLATION OF ALKYLIDENEMALONOMINIES AND TERM	Viole			Rofor-
			t lott	ç	4.00.00	00000
Compound Allylated	Alkylating Agent	Product	%	Цизо	Solvent	63116
GANDIO OVII O	, HD	CH.CH=C(C,H.)C(CH.)(CN),	93	NaOC <sub>3</sub> H <sub>7</sub> -i	$i.C_iH_iOH$	<b>‡</b>
(C2H5)2C=C(CN)2	CALSA C tr 7	CHICH-CIC.H.DCC.H.DCCN),	67	NnOC <sub>3</sub> H <sub>7</sub> ·i	i-C <sub>3</sub> II,011	211
	Orner	CH-CH-CK-H-)C(CH-CK-K)(CN)	81	NaOC <sub>2</sub> II <sub>5</sub>	Ethunol	215
(NO)O HOW HOW	CH R.	C.H.CH=C(CH,)C(C,II,)(CN),	1	NnOC,H,.i	i.C,H,OH	112
n-C3H 20(CH 3)==0(CN)2	C211555	C. H. CH = C(CH.)C(C, H.)(CN);	I	NaOC <sub>3</sub> H <sub>2</sub> ·i	$i.C_3H,OH$	
	$(C_2H_\delta)_2SO_4$	$C_2H_6CH=C(CH_3)G(C_2H_5)(CN)_2$	1	NaOC <sub>3</sub> II <sub>7</sub> ·i	i.C,II,OH	211
)=C(CN),	$C_2H_AI$	(1.Cyclohexenyl)othylmalononitrilo	63	NaOC <sub>3</sub> I1 <sub>7</sub> -i	i.C <sub>3</sub> II,0H	211
	CH.—CHCH.Br	(1-Cyclohexonyl)allylmalononitrilo	93	NaOC2113	Ethanol	215
$C_2H_3C(CH_3)=C(CN)$ .	CH3I	CH3CH=C(CH3)C(CH3)(CN)CO2C2II,	65	NaOC, II,	Ethanol	<del>1</del> 1
CO2C2H5		AT D COUNTY IS CONTRACT.	i:	Ma OC 15	Petrong	37
	C,H,I	$CH_3CH = C(CH_3)C(C_2H_3)(CN)CO_2C_2H_3$	00	INICO2113	TO HOUSE	3 1
	n.C,H,I	$CII_3CH=C(CH_3)C(C_3H_7-n)(CN)$ -	ij	NaOC2H5	Ethanol	37
		CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>				
	CH2=CHCH2Br	CH3CII=C(CH3)C(CH2CII=CII2)(CN)-	#	NnOC,II's	Ethunol	<del>+</del>
		$CO_2C_2H_5$				
	CH,=CCICH,CI	Structuro not determined*	Poor	NnOC,II,	Ethnool	<del>*</del>
•	CH, CBrCH, Br	Structuro not dotermined *	Poor	NaOC,II,	Ethnuol	<del>1</del> 50
	n-C,H,I	$CH_3CII = C(CH_3)C(C_4H_3 \cdot n)(CN)$	Ģ	NnOC,IIs	Ethunol	37
	•	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>				
	CH,CH=CHCH,Br	$CH_1CH = C(C1I_3)$ .	30	NnOC2Hs	Ethanol	<b>1</b> :0
		C(CH,CII—CHCH,)(CN)CO,C,II,				
	$CH_2 = C(CH_1)CH_2CI$	CH <sub>3</sub> CH=C(CH <sub>3</sub> ).	20-35	NnOC2II's	Ethanol	70
		C[CH2C(CH3)=CH2](CN)CO2C2U3				
	C,H,CH=CHCH,Br	$CH_3CII = C(CII_3)$	Poor	NaOC,II's	Ethnnol	<del>1</del> :0
	,	C(CH2CH=CHC4H3)(CN)CO2C2H3				

									,,,	7413 74	TIRILES	;
37	37 37 41	37	17	37	37	37	37	12		37	995	
Ethanol	Ethanol Ethanol CH,OH	Ethanol	NaOC <sub>3</sub> H <sub>7-i</sub> i.C <sub>3</sub> H <sub>7</sub> OH	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	Ethanol	
NaOC.H.	NaOC,H, NaOC,H, NaOCH,	NaOC <sub>2</sub> H <sub>5</sub>	NaOC3H7.i	NaOC <sub>2</sub> H <sub>3</sub>	NaOC <sub>2</sub> H <sub>5</sub>	NaOC.Hs	NaOC, H,	NaOC, Hs	NaOC,Hs	NaOC.Hs	NaOC,H,	
89	41 63 17	45	73	£3.	ĈĮ.	0#	87	70	57	63	ឡ	
$C_2H_3\mathrm{CH}{=}\mathrm{C}(\mathrm{CH_3})\mathrm{C}(\mathrm{CH_3})(\mathrm{CN})\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_3$	C <sub>2</sub> H <sub>5</sub> CH=C(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>5</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> CH=C(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>5</sub> )(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> CH=C(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>5</sub> )(CN)CO <sub>2</sub> CH <sub>2</sub>	C,H,CH==C(CH,)C(C,H,)(CN)CO,C,H,	C,H,CH=C(CH,)C(C,H,)(CN).	C <sub>2</sub> H <sub>3</sub> CH=C(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>7</sub> ·n)(CN). CO,C.H <sub>4</sub>	C <sub>2</sub> H <sub>5</sub> CH=C(CH <sub>3</sub> )C(C <sub>3</sub> H <sub>2·1</sub> )(CN). CO <sub>3</sub> C <sub>3</sub> H.	C <sub>2</sub> H <sub>3</sub> CH=C(CH <sub>3</sub> )C(CH <sub>2</sub> CH=CH <sub>2</sub> )(CN).	CH,CH=C(C,H,)C(CH,)(CN)CO,C,H;	$CH_3CH = C(C_2H_3)C(C_2H_3)(CN).$	$CH_3CH = C(C_2H_3)C(C_3H_7 \cdot n)(CN)$ .	CH,CH=C(C,H,)C(C,H,·i)(CN). CO_cC,H,	o <u></u> 2	of product.
CH,I	C,H,Br C,H,I C,H,I	$(C_2H_5)_2SO_4$	(C2H3)2SO3	$n ext{-}\mathrm{C}_3\mathrm{H}_7\mathrm{I}$	i-C3H,I	CH2=CHCH2Br	$_{ m I}^{ m r}$	$C_2H_3I$	$n$ -C $_{ m 3}{ m H}_{ m 3}{ m Br}$	i.C,H,I	$C_2H_3I$	So are on pp. 322–331.  I precluded purification Partially on distillation
$n \cdot C_3H_7C(CH_3) = C(CN) \cdot CO_2C_2H_5$	$n \cdot C_3 H, C(CH_3) = C(CN).$ $CO_3 CH_3$	$n \cdot C_{3}H_{7}C(CH_{3}) = C(CN) \cdot CO_{2}C_{2}H_{3}$	$n \cdot C_3H_rC(CH_3) = C(CN)$ . $CO_2C_3H_r$ .	$n$ - $C_3H$ , $C(CH_3)$ = $C(CN)$ - $CO_2C_2H_3$		•	$(C_2H_3)_1C = C(CN)$ . $CO_2C_2H_3$			CH,	$ \begin{array}{c c} CH_{i} & CO_{i}C(CN). \\ CH_{i} & CO_{i}C_{i}H_{s} \end{array} $	Jose: References 577-1080 are on pp. 322-331. * The poor yield obtained precluded purification of product. † The product isomerized partially on distillation

† The product isomerized partially on distillation.

TABLE IX—Continued

ALKYLATION OF ALKYLIDENEMALONONITHIES AND ALKYLIDENECYANOACETIC ESTERS

Refor-	nt enco	,01I 995	ol 37	ol 37	ol 41	11 37		6/6 HO	ol 996, 997	ol 259	ol 215	10l 259	,0Н 247
	Solvent	::C,H,	Ethanol	Ethanol	Ethanol	CIIOII		1.C,11,UF	Ethanol	Ethanol	Ethanol	Ethanol	; ;-C,H
	Base	NaOC,H;-i i.C,H,OII	NaOC, Hs	$NnOC_2H_5$	NaOC <sub>2</sub> H <sub>3</sub>	NaOCIIs	NaOCH,	NaOC,11,.1	$NnOC_2II_5$	NaOC,II's	NaOC <sub>2</sub> II's	NaOC,H,	NaOC3H,-i i-C3H,OH
Yiold.	%	09	78	70	7.9	97	32	1.7	l	45	7.9	09	52
	Product	$CH_2 \\ \nearrow CHCC(C_2H_3)(CN)CO_2C_3H_7 \cdot i \\ CH_2 & \parallel \\$	$n.C_3H_2CH==C(CH_3)C(CH_3)(CN).$	$co_2c_3H_6$ $n.c_3H_7CH=C(CH_3)C(C_2H_3)(CN)$ .	$CO_3C_2H_3$ $i:C_3H_3CH=C(CH_3)C(CH_3)(CN)$ .	CO2C;H; i.C,H;CH==C(CH,)C(CH,)(CN)CO,CH,	i.C,H,CH=C(CH,)C(C,H;)(CN)CO,CH,	$CH_2 = C(CH_3)CH = C(CH_3)$ .	Ethyl mothyl (I-cyclohoxonyl).	cynnoacetato Ethyl ethyl-(I-eyclohexonyl).	eyanoacctato Ethyl allyl-(1-cyclohoxonyl)-	cyanoncotato Ethyl n-butyl-(1-cyclohexenyl)-	eyanoacotato Ethyl (2-mothyl-2-cyclo- pontenyl)-(1-cyclohoxenyl)-
Abkybation of Abhilland	Alkylating Agent	$(G_2H_5)_2SO_4$	CHJ	$C_2H_5I$	CH <sub>3</sub> I	CH <sub>3</sub> I	$C_2H_sI$	CH <sub>3</sub> I	$CH_3I$	$C_2H_sI$	CH2=CHCH2Br	$n$ - $C_4$ $H_6$ $I$	2-Mothyl-2-cyclo- pentenyl bromido
ADK	Compound Alkylated	CH <sub>2</sub> CH <sub>2</sub> CHC=C(CN)- CM CO,C,H,-i	$_{n\text{-}C_{4}H_{1}C(CH_{3})=C(CN)}.$	CO2C2H5	:C,H,C(CH3)=C(CN).	$CO_2C_2H_5$ $i:C_4H_5C(CH_3)=C(CN)$ .	$CO_2CH_3$	$(CH_3)_2C=CHC(CH_3)=$	C(CN)CO <sub>2</sub> C3H7.* Ethyl cyelohoxyl-	ideneeyanoacotato			

			.1.	ני עננו	4 17 17 1	TWI	TOM	OF	ESTE	KKS A	IND	NIT	RILI	ES	
259	37	<b>4</b>	37	37	<del>1</del> 9	7	37	37	353	353	353	266	7.	: #	
Ethanol	СН3ОН	Ethanol	сн,он	Tolucno	Ethanol	Ethanol	CH3OH	Ether	Ethanol	Ethanol	Ethanol	Ethanol	C,H,	C <sub>t</sub> H,	
NaOC <sub>2</sub> H <sub>5</sub>	$NaOCH_3$	NaOC,H,	NaOCH3	NaNH <sub>2</sub>	NaOC, Hs	NaOC, Hs	NaOCH,	Na	NaOC, Hs	NaOC, Hs	$NaOC_2H_5$	NaOC.H.	Na	Na	
10	133	62	18	13	20-35	81	78	58	ì		ļ	1	I	1	
$n \cdot C_b H_{11} C H = C H C (C_b H_b \cdot n) (CN)$	$n$ - $C_4H_5$ CH= $C(CH_3)C(CH_3)(CN)$ - $CO$ - $CH$ -	$n \cdot C_4 H_3 \text{CH} = C(\text{CH}_3) C(\text{CH}_3)(\text{CN})$ .	$n \cdot C_4H_s$ CH==C(CH <sub>3</sub> )C(C <sub>2</sub> H <sub>5</sub> )(CN).	$n \cdot C_4 H_b CH = C(CH_3)C(C_2 H_3)(CN)$ .	$n \cdot C_1H_1 \text{CH} = C(\text{CH}_3)$ .  C(CH. C(CH. ) — CH $\cdot C$ CH	$C_2H_3CH=C(C_3H_7-n)C(CH_3)(CN)$ .	$C_2H_5CH=C(C_3H_7\cdot n)C(C_2H_5)(CN).$	$C_2H_3CH=C(C_3H_7\cdot n)C(C_2H_3)(CN).$	Ethyl methyl (2-methyl-1-cyclo- bexenylleynnogetet	Ethyl methyl-(3-methyl-1-cyclo-hexenyl)cyanoacetate	Ethyl methyl-(4-methyl-1-cyclo- hexenylleyanoacotate	Ethyl phenacyl-(4-methyl-I.	$C_6H_8CH=C(CH_3)C(C_2H_5)(CN)$ .	CH <sub>3</sub> CH=C(C <sub>6</sub> H <sub>5</sub> )C(C <sub>2</sub> H <sub>5</sub> )(CN). CO <sub>5</sub> C <sub>5</sub> H.	
$n$ -C $_4$ H $_9$ I	$CH_3I$	CH <sub>3</sub> I	$C_2H_5I$	$(C_2H_5)_2SO_4$	CH2=C(CH3)CH2CI	$CH_2I$	C <u>.</u> E.I	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> SO <sub>4</sub>	$_{ m I}^{ m cH}$	CH <sub>3</sub> I	$_{ m cH_3I}$	$C_6H_5COCH_2Br$	$\mathrm{C_2H_5X}_{\updownarrow}^{\updownarrow}$	$C_2H_5X_{\updownarrow}^{\dagger}$	080 are on m 299
$n \cdot C_6 H_{13} CH == C(CN) \cdot CO_6 C_6 H_6$	$n \cdot C_b H_{11}C(CH_3) = C(CN) \cdot CO_5CH_3$	n-C,H <sub>11</sub> C(CH <sub>3</sub> )==C(CN)- CO,C,H,	$n$ ·C <sub>s</sub> $\hat{\mathbf{H}}_{11}\hat{\mathbf{C}}(\hat{\mathbf{CH}}_3)$ =C(CN)- CO <sub>2</sub> CH <sub>3</sub>	•	$n \cdot C_b H_{11}C(CH_3) = C(CN)$ . $CO_2C_2H_b$	$(n\cdot C_3H_7)_2C$ ==C(CN)- CO $_2C_2H_5$	$(n \cdot C_3H_7)_2C = C(CN) \cdot CO_2CH_3$		Ethyl 2-methylcyclo- hexylidenccyanoacetate	Ethyl 3-methylcyclo. hexylidenceyanoacetate	hexylidenecyanoacetate		$C_{s}H_{s}CH_{z}C(CH_{s})=C(CN)$ . $CO_{z}C_{z}H_{s}$	C,H,C(C,H,S)==C(CN). CO <sub>2</sub> C <sub>2</sub> H,	Note: References 577-1080 are on nn 289

The relevances 577-1080 are on pp. 322-331.

† The product isomerized partially on distillation. The halogen was not specified.

## TABLE IX-Continued

ESTERS ESTERS	ALKYLIDENECYANOMOZII	Yield,
TABLE IX-COMMUNICATION	ALKYLIDENECKANOLOGICAL AND ALKYLIDENECKANOLOGICAL	ALKYLATION OF ALKYLIDENEMALOWS

Rofor-

oneo	181	181 181	217	181 181	181	181		Ċ	866	
Solvent	Ethanol	Ethanol Ethanol	Ethanol Ethanol	Ethanol Ethanol	Ethanol	Ethanol			$C_6H_6$	
Baso	NaOC2Hs	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOC <sub>2</sub> H <sub>5</sub>	NaOC2HS NaOC2HS	NaOC <sub>2</sub> IIS	NaOC2Hs			NaOCH3	
Yield,	% 02	11	09	36 65	1	5			55	
	Product Product Trily, mothyl-(3-indenyl)cynnoncetato	Ethyl othyl-(3-indonyl)cyanoacotato	Ethyl n-propyl-(3-indenyl)cynno- Ethyl isopropyl-(3-indonyl)cynno-	Ethyl allyl-(3-indenyl)cyanoacotato	Ethyl i.butyl-(3-indenyl)cyanoacetato	Ethyl i.amyl-(3-indenyl)cyanoacotato Ethyl mothyl-(2-indenyl)cyanoacotato	CH2CO2C2H3	NCCCO,C,H6		
ALKYLATION OF THE	Alkylating Agont	CH <sub>3</sub> I	.C <sub>3</sub> H,I	CH3=CHCH2Br	CH2=CHCH2I	1.C,H11 1.C,H11	CHIT			$ClCH_2CO_2C_2H_5$
АБКЛ	Compound Alkylated	Ethyl 1 indanylidono. oyanoacotato					Ethyl 2-indanyl- ideneeyanoacotato§	H.O.Ookoo		

§ This ester may be ethyl 2-indenyleyaneacetate as designated in ref. 181.

TABLE X

ALKYLATION OF MALONONITRILE AND MONOALKYLMALONONITRILES, RCH(CN)<sub>2</sub>

				Yield,			Refer-
R	Alkyla	Alkylating Agent	Product	%	Base	Solvent	ence
		$c_{_1}$					
Н		CH3I	$(CH_3)_2C(CN)_2$	Poor	Dry silver salt	None	104
		1 120	/(CH <sub>3</sub> ) <sub>2</sub> C(CN) <sub>2</sub>	ca. 14	NaOCH,	$CH_3OH$	104
		Unigi	(CH <sub>3</sub> ) <sub>2</sub> C(CN)C(=NH)OCH <sub>3</sub>	55			
		CH,I	(CH <sub>3</sub> ) <sub>2</sub> C(CN) <sub>2</sub>	36	NaOC <sub>2</sub> H <sub>5</sub>	None	104,999
		CHCl <sub>3</sub>	(NC) <sub>2</sub> CHCH=C(CN)C(=NH)OC <sub>2</sub> H <sub>5</sub>	i	$NaOC_2H_5$	Ethanol	231
		$C_2$					
		$C_2H_3I$	$(C_2H_3)_2C(CN)_2$	32	NaOC,H,	None	104, 999
		C,H,I	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> C(CN)C(=NH)OC <sub>2</sub> H <sub>5</sub>	Good	NaOC2Hs	Ethanol	104
		C,-C,	$((C_2H_5)_2C(CN)_2$	i			
		n.C.H.Cl	(WO)CH D'C		11 00 11	į	c c
		יייייייייייייייייייייייייייייייייייייי	(N-03+1)/20(01/2)	1	NaOC2Ds	Ethanol	999
			(CeHsCH <sub>2</sub> ) <sub>2</sub> C(CN) <sub>2</sub>	1	Na	Ether	95
		Conscient	$(C_bH_3CH_2)_2C(CN)_3$	32	$NaOC_2H_5$	Ethanol	95, 999
1		2,3-Dibromoindono	Bromoindonylmalononitrile*	100	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	781
בייני הייני		Con CH2CI	C,H,CH,C(C,H,)(CN)C(=NH)OC,H,	7.1	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	95
: 17 <sup>8</sup> 2			CollsC(CH3)(CN)C(=NH)OC2H3	ca. 100	NaOC2H5	Ethanol	333
			C(CH <sub>2</sub> ),C(C,H <sub>5</sub> )(CN),	40	$NaOC_2H_5$	Ethanol	1000
C.H.CH	THE.	CH I	Censchol(C,Hs)(CN)	100	$NaOC_2H_5$	Ethanol	333
(		CH T	Constitution (CN)	ţ	Dry sodium salt	None	95
		CH I	C,H,CH,C(CH,)(CN),	92	Dry silver salt	Ether	95
		C,H,I	C,H,CH,C(CH,)(CN)C(=NH)OC,H,	85	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	95
;	i	,	Carisonio (C2Hs)(CN)C(=NH)OC2Hs	75	NaOC <sub>2</sub> H <sub>5</sub>	Ethanol	95
010	12010-010	COC+ 1111 10020					

Note: References 577-1080 are on pp. 322-331,
• The structure of this product was not determined.

#### ABLE XI

ATHALACTION OF MONOGARDOXYLIG ESTERS, RCH(R.)CO2R"

Refer-	ence	196	88	69 196	240	504	81	10	83, 81	178	i		69	98	69		8	818	81	89	89	
	Solvent	Ether	Ether	Ether	Ether Ether	Ethanol	CH3CH(0C2H5)2	1-Butoxy-2- othoxyethano	CH3CH(OC3H7-n)2	Ethanol	Cons		Tither	Ether	Ether	Euler		Ether	1-Butoxy-2-	ethoxyethane	Ether	Educk
·	Baso	¥	NaC(C,Hs)3	NaC(C, H5)3 NaC(C, H5)3	,	$NaOC_2H_5$	жон	кои	жон		NaNH <sub>2</sub>		1	NaC(Cans)3 NaC(CaHs)3	NaC(CoH6)3	$NaC(C_6H_6)_3$		NaC(CgH5)3	HOH	WOR	NaC(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub>	NaC(C <sub>6</sub> H <sub>5</sub> )3
dicated,	Yleld, %	, L	Poor	젊문		1 1	<u>t</u>	38	00 (50)	00 1	7	20		26 55	58	55		30	233	<b>4</b>	42	61
KYLATION OF MICKOCHINE OTHER STATES INDICATED.)		Product	n.C3II,CO2C2II6	G_II(CII_2)_CU_2C_2H_5 ;.CIICII(C_1II_5)CO_2C_2H_5	Call, CH(Calls) CO2 C2Hs	$C_{0}H_{5}CH(C_{2}H_{5})CO_{2}C_{2}H_{5}$ $C_{0}H_{5}CH(C_{2}H_{5})CO_{2}C_{2}H_{5}$	Ethyi 1-methyi-4-phenyipherida 4-carboxylate	$(c_2\Pi_5)_2N(c\Pi_2)_2C\Pi(C_6\Pi_5)CO_2C_2\Pi_5$	C6115 C12 C12 C	$\mathrm{C_6H_5CH_2CH(C_6H_5)CO_2C_2H_5}$	None (Ethyl α-phenyl-α-(7-chloro-	4-quinolyl)acetate	4-quinolyl)acetamide	$c_2^{}\mathrm{H}_6^{}\mathrm{O}_2^{}\mathrm{CC}(\mathrm{CH}_3)_2^{}\mathrm{C}(\mathrm{CH}_3)_2^{}\mathrm{CO}_2^{}\mathrm{C}_2^{}\mathrm{H}_6^{}$	$(CH_3)_3CCO_2C_2H_5$	C1H <sub>5</sub> C(CH <sub>3</sub> )2C2C2C3 CH <sub>2</sub> CH <sub>2</sub> C(CH <sub>3</sub> )2		OO	C.H.CH.C(CH3)2C(	Canson Constant	H J ON ( 110% 200	Canscans/Canssacs_1 n-c3H,C(CH3)(C2H5)CO2C2H5
ALKYLATION OF MONOGEN		Alkelating Agent	C.11.Br	C6.115,C11	$c_{211,5}^{1}$ $c_{211,5}^{1}c_{3}c_{2}^{1}$	C,11,13C	CII3N(CII2CII2CI)2	$(C_2\Pi_5)_2N(C\Pi_2)_2Cl$	Canscilaci	C_111,C11,C1	C,110,011	4,7.Dichloro	dinnonne	1	cir <sub>3</sub> 1	$c_2 \pi_s I$	CH <sub>2</sub> —CH <sub>2</sub>	. ,0,	(CH <sub>3</sub> ),CBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	C,H,CH,CI		$C_0H_5CH_2CI$ $n$ - $C_3H_7I$
			,a	==	4.C <sub>3</sub> 11,	Colts									CII3							C,III,

cII,

		Ethyl α,α-dl-(2-thlenyl)-γ- (4-morphollnyl)butyrato CH <sub>3</sub> O <sub>2</sub> CC(C <sub>B</sub> H <sub>3</sub> ) <sub>2</sub> C(C <sub>B</sub> H <sub>3</sub>	Good 300 300 300 300 300 300 300 300 300 30	Nanh;  Toluc  NaC(C <sub>6</sub> H <sub>6</sub> ) <sub>3</sub> Ether  Nanh;  (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CCN]Nn  (C <sub>6</sub> H <sub>6</sub> )  Nanh;  ((C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CCN]Nn  ((C <sub>2</sub>	Toluene  Liquid NH3  Ether  Cellier  Cellie  C	1002 67 1003 62 1004 62 93 564 67 61, 1005 93 01, 93
	C <sub>4</sub> II <sub>3</sub> CHBrCO <sub>3</sub> CH <sub>3</sub> β(2-Nethyl-5-ethyl- I-pheridyl)propyl	pperuy)yateate CII3o2CORCa(I3OCICo,I3)CO2CII3* Ethyl a.z-diplonyl-y-(2-methyl- 5-ethyl-1-pheridyl)valerate	Poor	(C <sub>6</sub> H <sub>5</sub> )3CNa [(C <sub>6</sub> H <sub>5</sub> )2CCNJNa	Ether C <sub>6</sub> II <sub>6</sub>	
(C <sub>6</sub> H <sub>3</sub> )	ride gCIBr	(C <sub>4</sub> H <sub>3</sub> ),CHC(C <sub>6</sub> H <sub>3</sub> ),CO <sub>2</sub> CH <sub>3</sub> * (C <sub>6</sub> H <sub>3</sub> ),CC(C <sub>6</sub> H <sub>3</sub> ),CO <sub>2</sub> CH <sub>3</sub> *	11	NaC(C <sub>6</sub> U <sub>5)3</sub> NaC(C <sub>6</sub> U <sub>5)3</sub>	Toluene Ether	67

<sup>\*</sup> The nurthyl exter was used in this experiment.

The halogen was not specified.

The fennyl exter was used in this experiment.

The allyl exter was used in this experiment.

## TABLE XI-Continued

	Refer-	епес	248	248	248 248 248	248 248 248	248	248	91, 93	248 93	248 60 60	09	70 93
		Solvent	Ethanol-ether	Ethanol-ether	Ether Ether Ethanol	Ether Ether	istner Ether	Ether	C <sub>6</sub> H <sub>6</sub> ·C <sub>6</sub> H <sub>5</sub> Cl	Ether Ethanol-ether	Ether Ether Ether	Ether	Ether C <sub>6</sub> H <sub>6</sub> -C <sub>6</sub> H <sub>5</sub> Cl
$O_2R''$	÷	Dogo	H,	KOC2H5	KOC <sub>2</sub> H <sub>5</sub> KOC <sub>2</sub> H <sub>5</sub> KOC <sub>2</sub> H <sub>5</sub>	KOC2HS KOC2HS	KOC2Hs	KOC2HS KOC2Hs	[(C,H,),CCN]Na C,H.C,H,C	KOC <sub>2</sub> H <sub>5</sub> KOC <sub>2</sub> H <sub>5</sub>	KOC2Hs NaNH2 NaNH2	NaNH2	NaC(C <sub>6</sub> H <sub>5</sub> ), Ether [(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CCN]Na C <sub>6</sub> H <sub>6</sub> C <sub>6</sub> H <sub>5</sub> Cl
(R')C	icated	Yleld,	»	1	Good	1.1	i	1 1	40	£	65	1	48
TABLE AI—COMMING.  **COMMING RIGHTS, RCH(R')CO2R"	KYLATION OF MONOCARBOXXING LINES OF MICROSPECT.)		Product	Diethyl 2,3-bis-(o,o -diphenylene)-	Dietity Lastination of processing accordate Ethyl 9-nethylfluorene-9-earboxylate Ethyl 9-ethylfluorene-9-earboxylate	Diethyl a,a'-bls-(0,0 -ul)neus re-cy adlpate Ethyl 9-allylluorene-9-earboxylate	Diethyl α-(0,0'-diphenylene)glutarate Diethyl α-(0,0'-diphenylene)glutarate	None	9-carboxylate πthyl 9-[β-(4-morpholinyl)ethyl]-	fluorene-9-earboxylate fluorene-9-earboxylate Ethyl 9-benzylfluorene-9-earboxylate Ethyl 9-fe-(1-piperidyl)ethyl fluorene-	P-enrhoxylate Ethyl 9-phenocyfluorenc-9-enrhoxylate p-GH <sub>2</sub> C <sub>8</sub> H <sub>2</sub> C(CH <sub>2</sub> )CO <sub>2</sub> CH <sub>2</sub> C <sub>8</sub> H <sub>5</sub> + ord — CH CH + C(C, H, N(C, H, N(C, H, N(C, H, N)))	CO_CCH_CGH_C(C,H_1)(C,H_1CH_3-p)-	CO <sub>2</sub> CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> <sup>+</sup> (n.C,H <sub>3</sub> S) <sub>2</sub> C(CH <sub>3</sub> )CO <sub>2</sub> CH <sub>3</sub> * Ethyl c-plenyl-c-veratryl-γ- (4-morpholinyl)butyrate
	ALKYLATION OF	so réma aut)	Alkylating Agent	I2	12 CH3 C.H41	Br(CH <sub>2</sub> ) <sub>2</sub> Br CH <sub>2</sub> =CHCH <sub>2</sub> Br	CICH, CO, C, H,	C <sub>6</sub> H <sub>5</sub> I	2,4-Dinitro- bromobenzene	ethyl chloride CeHsCH2Cl	ethyl chloride chyl chloride C <sub>6</sub> H <sub>5</sub> COCH <sub>2</sub> Br CH <sub>3</sub> I	CH2=CHCH25F	CH <sub>3</sub> I β-(4-Morpholinyl)- ethyl chloride
			à	R 0,0'-Diphenylene							p-Tolyl		-C,H13 n-C,H1sI Veratryi
			ı	π 0,0'-Dij							Ħ	a 1	-C,H <sub>15</sub>

1006		2000
Ether		Ether Ether Ether
$\mathrm{NaC}(G_6\mathrm{H_5})_3$		NaC(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> NaC(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub> NaC(C <sub>6</sub> H <sub>5</sub> ) <sub>3</sub>
64	<b>r</b> -	129
$\begin{pmatrix} c_{1} \\ c_{1} \\ c_{1} \end{pmatrix}$	+ CO <sub>2</sub> H CH <sub>3</sub> O CH <sub>3</sub> O CH <sub>3</sub> O	$n$ - $C_{14}\Pi_{13}$ - $C(C\Pi_3)(C_1\Pi_{13}$ - $n)CO_2C\Pi_3^*$ $n$ - $C_{12}\Pi_{13}$ - $C(C\Pi_3)(C_{10}\Pi_{21}-n)CO_2C\Pi_3^*$ $n$ - $C_{12}U_{23}$ - $C(C_{21}\Pi_3)(C_{10}\Pi_{21}-n)CO_2C\Pi_3^*$
		,_

n-C<sub>11</sub>H<sub>31</sub> n-C<sub>11</sub>H<sub>30</sub> Cl n-C<sub>10</sub>H<sub>31</sub> n-C<sub>12</sub>H<sub>38</sub> Cl C<sub>2</sub> Note: References 577-1030 are on pp. 322-331.

The methyl ester was used in this experiment.

The benzyl ester was used in this experiment.

00						
	Reference	262 262 262	262 574 574, 1007, 1008	574 574 574, 1007, 1008	574, 1007, 1008	574
	Solvent	Ether Ethanol	Ether C,H,	Toluene Toluene Toluene	$C_{\rm e}H_{\rm c}$	Toluene
*, **, **, **, **, **, **, **, **, **,	Base	NaOC <sub>2</sub> H <sub>5</sub> KOC <sub>2</sub> H <sub>5</sub>	KOC <sub>2</sub> H <sub>5</sub> NaH NaH	N N N N N N N N N N N N N N N N N N N	NaH	Na
4	Yield,	 ca. 100	85 80 42 68	24	99	16
TABLE XII ALEYLATION OF 3-ARYL-2-BENZOFURANONES TO	R in Product	$C_{iH_5}$	-C,H, -CH,CH=CH, -(CH,),Cl -(CH,),CN	$\begin{array}{l} -(\mathrm{CH}_2)_2 \mathrm{N}(\mathrm{CH}_3)_2 \\ -(\mathrm{CH}_2)_2 \mathrm{N} \mathrm{HC}_4 \mathrm{H}_9 \cdot n \\ -(\mathrm{CH}_2)_2 \mathrm{N} (\mathrm{C}_2 \mathrm{H}_5)_2 \end{array}$	eta-(4-Morpholinyl)ethyl	$-(\mathrm{CH}_2)_3\mathrm{N}(\mathrm{C}_2\mathrm{H}_5)_2$
ALRYLATION OF 3-A	Alkylating Agent	T <sub>2</sub>	$CH_3I$ $C_2H_5I$ $CH_2=CHCH_3Br$ $Br(CH_2)_3CI$ $Br(CH_2)_3CN$	(CH <sub>2</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl n-C <sub>4</sub> H <sub>5</sub> NH(CH <sub>2</sub> ) <sub>2</sub> Cl (C <sub>4</sub> H <sub>5</sub> ) <sub>3</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl	$\beta$ .(4-Morpholinyl)ethyl chloride	, arr word Br

1008

1007, 1008 574, 1007, 1008	262 574 574, 1007.	1008	57.4, 1007, P	1.24	1.58	1007, 674,	1007, 1001 1007, 1004		12.1. 1007.	1008 574, 1007.
Tolueno Toluene	Toluene	Toluono	$C_{\mathfrak{a}}\Pi_{\mathfrak{a}}$	Toluone	Tohnene	0,114	:	Edhor	Tohrene	Tolueno
NaH NaH	Na Na	Na	NaII	N.	N.	Nall	i	Z.	Na	N.
80	ca. 100 78	17	2	1.1	88	63	1	ĝ	70	7.1
$\begin{array}{ll} -CH(\mathrm{CH_3})\mathrm{CH_2}\mathrm{N}(\mathrm{C_2H_5})_2 \\ -C\mathrm{H_2}\mathrm{CH}(\mathrm{CH_3})\mathrm{N}(\mathrm{C_2H_5})_2 \end{array}$		$\gamma$ -(4-Morpholiny·l)propy·l $-(CH_3)_4N(C_3H_5)_2$	$-CH_{2}C(CH_{3})_{3}CH_{2}N$	$(\mathrm{CH_3})_{\mathtt{a}}\mathrm{N}(C_{\mathtt{d}}\mathrm{H_6}.n)_{\mathtt{a}}$	$-(CH_2)_3N(C_4H_6\cdot n)_2$	$-(CH_2)_2N(C_4H_6\cdot n)CH_9C_6H_5$	$-(CH_2)_{11}N(C_2H_5)_2$ $C_6H_6$		$-(CH_2)_2N(C_2H_5)_3$	$-(GII_2)_2N(C_2II_6)_2$
$(C_2H_5)_2$ NCH $_2$ CH $(CH_3)$ Cl $(C_2H_5)_2$ NCH $(CH_3)$ CH $_2$ Cl	$C_{b}H_{s}GH_{2}Br$ $eta \cdot (1-Piperidyl)$ ethyl chlorido	$p.(4-Morpholinyl)$ propyl chlorido $(C_2H_5)_2N(CH_5)_4Cl$	OONCH,C(CH,),CH,CI	$(n\cdot C_4H_{\mathfrak{p}})_3N(CH_3)_3Cl$	$(n\cdot C_4H_s)_2N(CH_s)_3Cl$	$C_dH_s$ CH $_2N(C_1H_0\cdot n)(CH_2)_2$ Cl	$(C_4 1 T_5)_a N (C T T_4)_1 C T$ $C_4 T T_5$		$(C_2H_5)_2N(CH_2)_2GI$	$(C_2H_{\mathcal{E}})_2N(CH_2)_2Cl$
									<i>6</i> -0 <i>1</i>	5.13r

Notes Maderences 677-1080 are on pp. 322-331.

#### ORGANIC REACTIONS

				U	RGAN	10 14												
Dofor-	coco	122,1013 $323$	53	1014	122,1013	53, 122 1013 1013	323	53, 122, 1013	1015	323	1015	•	323	1017	323	23		
	Solvent	Paraffin off	Ether Ether	Ether	Tiher	ouses ouses	Liquid NIIs	Ether		Toluene Liquid NII3	Tolucne	Tolucne	Liquid NH2	Calle	Ethanol Llquld NH2	1	$C_6H_8$	
CH(R')CN	Yleid, Base	HNex	58 NaNH2	ca. 70 NaNH2 23 NaNH2	24 15	87 NaNH2 80-00 NANH2 NANH3		27 September 20 Se		80 NaNH2		57 Nanus 25 Nanus	a will.		NaOC2Hs	16-40	40 NaNH2	
TABLE ALV	ALEXLATION OF MONONITRILES, LOLLY, XIGIA, 2000 NO.	Product	(C <sub>2</sub> H <sub>6</sub> ) <sub>3</sub> CCN	(C,H,)2CHCN (C,H,)2CHCN	(0.14)2CHCN (0.14)2CHCN (0.45)3CCN	(CH <sub>2</sub> =CHCH <sub>2</sub> ) <sub>3</sub> CCN	CII, CHCH, CH, CN	CH2 CHOILE	NOTHOCH'O-W	(n-c, H, ), CHCN		(n-C <sub>5</sub> H <sub>11</sub> ) <sub>3</sub> CCN (n-C <sub>5</sub> H <sub>11</sub> ) <sub>3</sub> CCN	Di-(2-pyridy)	Concensor	None None	(Calchachach	((C, H, CH, S), CCN	Construction
	ALKYLATIO	Alkylating Agent	C2 C.H.C1	$c_2H_5$ Br	C <sub>2</sub> H <sub>3</sub> Br C <sub>2</sub> H <sub>5</sub> Br	$C_3$ - $C_6$	CH2 = CHCH2Cl	CH2 CHCH2Br	$n$ - $C_4H_0$ br	$n$ -C $_4$ H $_9$ Br	n-CallyBr	n-C4H,0SO2C4L(CH37)	2-Bromopyridine	C <sub>6</sub> -C <sub>7</sub>	Cansor Cansonio	Conscitor	C,H,CH,CI	Con CH CH CH

H H

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#### THE ALKYLATION OF ESTERS AND NITRILES

THE ALL	LIDALION	01 11011	11112	11222122	.~ -
71 71 323 1015 122 53 53 1018	53, 122, 1013 53	53, 122 53, 122 53, 122 122	75, 78 476, 478 1019, 1020, 1021	171 249 1015 1022	122 1015 1015
Ether G <sub>g</sub> H <sub>8</sub> Liquid NH <sub>3</sub> Toluene Dloxane G <sub>g</sub> H <sub>8</sub> G <sub>g</sub> H Toluene	Ether Ether	Ener G <sub>e</sub> H <sub>6</sub> n-C <sub>e</sub> H <sub>6</sub> Cl Ether C <sub>e</sub> H <sub>6</sub>	None None Liquid NH <sub>3</sub>	Liquid NH3 Inert solvent Toluene Liquid NH3-ether	C <sub>6</sub> H <sub>6</sub> Toluene Toluene
Na Na KNH <sub>2</sub> NaNH <sub>2</sub> NaNH <sub>3</sub> NaNH <sub>2</sub> NaNH <sub>2</sub>		NaNH2	42 NaOH — KOH 80-90 NaNH <sub>2</sub>	31 NaNH2 NaNH2 76 NaNH2 57 NaNH2	Sxeel- NaNH <sub>2</sub> lent . — NaNH <sub>2</sub> 81 62 NaNH <sub>2</sub>
1   2   2   2   3   1	77 3 65 113	E 88 8 1 1	4 1 9		H H H H H
C <sub>2</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CN Nono C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CN (n·C <sub>7</sub> H <sub>13</sub> ) <sub>2</sub> C(CH <sub>3</sub> )CN C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH(CH <sub>3</sub> )CN (C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH(CH <sub>3</sub> )CN (C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH(CH <sub>3</sub> )CN (C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH(CH <sub>3</sub> )CN n·C <sub>10</sub> H <sub>2</sub> CH(CH <sub>3</sub> )CN	((C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CHCN ((C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> CCN  n-G <sub>2</sub> H <sub>7</sub> CH(C <sub>2</sub> H <sub>8</sub> )CN (n-C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>8</sub> )CN	i-C,u,GH(C,u,S)CN (CH1,=GHCH1,S)C(C,u,S)CN n-C,11,GH(C,u,S)CN C,u,O(CH2,2CH(C,u,S)CN C,u,O(GH3,2CH(C,u,S)CN	Cyclopropancearboultille Cyclopropancearboultille Cyclopropancearbonitrile	$(CH_2 = CHCH_2)_2(CH = CH_2)CN$ $n \cdot C_3H_7CH(C_2H_3)CN$ $(n \cdot C_3H_7)_2CON$ $2 \cdot Methylcyclopropane$ carbonitrile	$CII_{2} = CHOH_{2}C(c_{2}H_{5})_{2}CN$ $\begin{cases} (n \cdot C_{4}H_{9})_{2}CHCN \\ (n \cdot C_{4}H_{3})_{3}CCN \\ (n \cdot C_{7}H_{13})_{2}C(C_{4}H_{9}-n)CN \end{cases}$
C2-C10 C2-U1	C <sub>2</sub> -C <sub>8</sub> C <sub>2</sub> H <sub>5</sub> Dr n-C <sub>5</sub> H <sub>7</sub> Br	+C <sub>3</sub> H <sub>3</sub> Br CH <sub>3</sub> =CHCH <sub>2</sub> Cl n-C <sub>4</sub> H <sub>3</sub> Cl C <sub>4</sub> H <sub>3</sub> O(CH <sub>2</sub> ) <sub>2</sub> Cl C <sub>4</sub> H <sub>2</sub> O(CH <sub>3</sub> ) <sub>3</sub> Br	None None None	CH <sub>2</sub> =CUCH <sub>2</sub> Dr (C <sub>2</sub> H <sub>2</sub> ) <sub>2</sub> SO <sub>4</sub> n-C <sub>3</sub> H <sub>7</sub> Dr None	C <sub>2</sub> II <sub>5</sub> Br n·C <sub>4</sub> II <sub>9</sub> Br n·C <sub>4</sub> II <sub>15</sub> Br
СИ3	$C_2H_5$		cicii <sub>2</sub> cii <sub>2</sub>	$CII_2 = CII$ $n \cdot C_3 II_1$ $CICII_2 CII(CII_3)$	$\operatorname{CH}_2 = \operatorname{CHCH}_2$ $n \cdot \operatorname{C}_4 \operatorname{H}_{\bullet}$

Note: References 577-1080 are on pp. 322-331.
• The halogen was not specified.

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TABLE XIV	
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	Refer-	спео	59 53, 1013	254	•	187	1023	187		187	187		171	1015	254		254	254	69	254
		Solvent	Ether C.H.		CeII	Toluene	mollicut		CH3CH(OC4118-11/2	Dioxane	Toluene	Tolueno	Ether	Toluene	,	Toluene	Toluene	C.H.	, ,	C <sub>6</sub> H <sub>6</sub>
74.4	N.		base NaNH2	NaNH2	NaNH2	11.6	Nan H2	NaNH <sub>2</sub>	кон	NaOCHa	LINH,	NaNHa	NaNH2	NaNH2		NaNH2	NaNH2		Nanus	NaNH2 NaNH2
	I(K)	Yleld,	ر ا %	70	42		9	48	5.4			99	38			31	48		40	18
TABLE XIV-Continue	MONONITRIES, RCH(K')CIN		Product	CoH CH CH (C(Ho-n)CN	(n-Cgariff) CH(CaH3S)CN	(0113)21.	2.Thienyl-(2-cyclo-	pentenyi)acetonikiio Gwelohexyl-(2-thienyi)-	acctonitrile		ĊÌ			$CH_3CH = C(C_2H_5)^*$ $CH(CH_2CH = CH_2)CN$	$\begin{cases} (C_2H_5)_2NGH_2GH(C_4H_9^{-n})_2GN \\ (C_3H_5)_2NGH_2G(C_4H_9^{-n})_2GN \end{cases}$	(CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> CH(C <sub>6</sub> H <sub>6</sub> S)CN	(CH3),N(CH2),CH(C3H4N)CN		(CH <sub>2</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> CH(C <sub>5</sub> H <sub>4</sub> N)CN	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH(C <sub>6</sub> H <sub>13</sub> ·n)CN (CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> CH(C <sub>6</sub> H <sub>11</sub> )CN
t.	,	ALKYDAIN	Antendating Agent	C.H.CH2Cl	$n$ ·C <sub>8</sub> $\Pi_{17}$ $ar{ ext{Dr}}$	$(CH_3)_2N(CH_2)_2Cl$	Theorem 1	chloride	Cyclohexyl bromine	2.Cyclohexenyl bromido	2.Cyclohexenyl bromide	o.Cvelolexenyl bromldo	2.Cyclohexenyl bromide	CH2=CHCH2Br	n.C.HgBr	CH.).NCH.CI		(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> C.	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl	Coh CH2CI (CH3)2N(CH3)2CI
				R'	n-C4H2 (Com.)		\s\ (≡C,II <sub>3</sub> S)							$_{\mathrm{CH_3CH}}\!=\!\mathrm{C}(\mathrm{C_2H_6})$	(C,H,),NCH2		S CH2		L	"N" "- "N" "- " " " " " " " " " " " " "

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	4 0 THE	27111	YINVII	<b>Ω1</b> /	, Or		. U.		•~	-3	- 1 4		-,			6		10		
171	256,1024 1025 1026,806 583 1027, 1028	195	359, 992 76 231		\$ \$ \$ \$	1025	1029	1030, 1031	1032	84	564	1033	1034	1035	1036	249, 359	305	306, 305	307	305
Liquid NH3-ether	Ethanol Líquid NH <sub>3</sub> None Ether Ether	Liquid NH3-ether	Bther None Ethanol		H <sub>5</sub> )30H H <sub>2</sub> 0 H-),10H H <sub>2</sub> 0		Liquid NH3	Ether	Сви	тот по	Ethanol	None	Ether	Ether	Toluene	Ether	Ether	Ether	$C_6H_6$	Ether
$NaNH_2$	NaOC <sub>2</sub> H <sub>5</sub> Na NaNH <sub>2</sub> NaNH <sub>2</sub>	$NaNH_2$	NaNH2 NaOH NaOC2H6		[C,H,CH,CH,N(C,H,),10H		$NaNH_2$	$NaNH_2$	NaNHa	CoH,CH,N(C		NaNH2		$NaNH_2$	NaNH2	NaNH	NaN H2	NaNH2	$NaNH_2$	NaNH <sub>2</sub>
10 40	68-72 66 66	20	67 31		Good	ן ו	1	81	98	1	Poor	ì	70-80	!	65	83	4.4	38	51	39
$\begin{cases} CH_2 = CHCH_2CH(C_6H_9)CN \\ [(CH_2 = CHCH_2)_2C(C_6H_9)CN \end{cases}$	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>4</sub> )CN C <sub>6</sub> H <sub>5</sub> CH(CH <sub>5</sub> )2N	(C,H,CH(CH3)CN	$C_6H_5C(C_{H_3})_2CN$ $C_6H_5CH(C(C_{H_3})_2CN$ $C_6H_5CH(C(C_N))_CH_2CH(C_6H_5)_CN$ $C_6H_5CH(C(C_N))_CH=C(C_6H_5)_CN$	C(=NB)OC2HS	C <sub>6</sub> H <sub>5</sub> CH(C <sub>2</sub> H <sub>5</sub> )CN	C,H,CH(C,H,)CN	C,H,CH(C,H,)CN	C,H,CH(C,H,)CN	CAH,CH(C,H,)CN	None	Censch(C2H5)CN	C,H,CH(C,H,S)CN	C,H,CH(C,H,)CN	Conscient Consci	C, H, C(C, H,), CN	C,H,CH(C,H,)CN	1-Phenylcyclopropane- 1-carbonitrile	1-Phenylcyclopropane-	1-Phenyleyclopropane-	HO(CH <sub>2</sub> ) <sub>2</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN
$\begin{array}{ll} \text{-Cyclohexenyl} & \text{CH}_2 \! = \! \text{CHCH}_2\text{Br} \\ (=\! \text{C}_0\text{H}_9) & \text{CH}_2 \! = \! \text{CHCH}_2\text{Br} \end{array}$	C <sub>1</sub> CH <sub>3</sub> I	1 #20	$(\mathrm{CH}_3)_2\mathrm{SO}_4$ $\mathrm{CH}_3\mathrm{I}_2$ $\mathrm{CHCI}_3$	ė	C2HsCI	Canebi C.H.Br	C,H,Br	$c_2^-$ H $_5^6$ Br	C,H,Br	$C_sH_sI$	$c_2^{-}$ H $_5^{-}$ I	C <sub>2</sub> H <sub>5</sub> I	$C_2H_5I$	$C_2^-H_5^-I$	$C_2H_{\delta}I$	$(C_2H_5)_2SO_4$	CI(CH <sub>2</sub> ) <sub>2</sub> Br	Br(CH <sub>2</sub> ) <sub>2</sub> Br	Br(CH <sub>2</sub> ) <sub>2</sub> Br	$\mathrm{HO}(\mathrm{CH_2})_2\mathrm{Cl}$ Note: References 577-1080 are on pp. 322-331.
J-C) (=)	C,Hs																			Note: References

#### ORGANIC REACTIONS

TABLE XIV-Continued

## ALKYLATION OF MONONITRILES, RCH(R')CN

	OF TAINTS	THE THE TAX AND THE PARTY OF TH	•	•		Dofor
			Yleld,		Solvent	ence
	Alkylating Agent	Product	ર	Dated		1001
	ITO(CIT,),CI	None	1 1	NaNH <sub>2</sub>	Toluene	1037
<b>⊸</b> Ø.		noich <sub>2</sub> ),ch(c <sub>4</sub> H <sub>5</sub> )cn	30	NaNH	Liquid NH3	1037
ប័						
ā	.C.11.13r	None	ł	NaOM	None	270
Ė	n·C <sub>3</sub> II <sub>7</sub> Br	n-C3H,CH(C4H5)CN	70-80	NaNH <sub>2</sub>	Ether	1031, 359, 1034,
						1035
÷	n-C,II,Br	(n-C,II,),C(C,II,)CN	00	NaNII.	Tolueno	1036
k	c,n,x•	n.C, H,CH(C,H,)CN	j	Na	Liquid NH3	1025
÷	c,ii,i	n-C, II, CII (C, IIs) CN	ł		None	279,79,
÷	.C <sub>3</sub> Π <sub>γ</sub> Br	·c,H,CH(C,H,)CN	70-80	NaNH2	Ether	1031, 566
CH	CH,=CHCH,Br	CH,=CHCH,CH(C,H,)CN	30	NaNH,	Ether	00
č	C(CII,),I	1-Phenylcyclobutane-	18	Na .	Ether	92
		1-carbonitrile	,	!	ŝ	***
CI	chjembrem, br	1-Phenyl-2-methylcyclopropane- 1-carbonitrile	18	NaN H <sub>2</sub>	Etner	305
ă	Br(CH2),Br	1-Phenylcyclebutanc-	15	NaNH2	Ether	300
		1-carbonitrile	•			
1(0	I(CII <sub>2</sub> ) <sub>3</sub> I	1-Phenylcyclobutane-	30	ł	Ether	92
C		reginaling				
CD	CH <sub>2</sub> OCH <sub>2</sub> O(CH <sub>2</sub> ) <sub>2</sub> Cl	[CH30CH20(CH2)]2C(C6H3)CN	13	NaNH <sub>2</sub>	CaHa	1038,
Ė	n-C,III,Br	n-CAH,CH(CAH,)CN	j	NaNII,	None	142
				•		

#### THE ALKYLATION OF ESTERS AND NITRILES

n-C <sub>4</sub> H <sub>9</sub> Br n-C <sub>4</sub> H <sub>9</sub> Br n-C <sub>4</sub> H <sub>9</sub> Br o-C <sub>4</sub> H <sub>9</sub> Br	n-C,H,CH(G,H,S)CN (n-C,H <sub>0</sub> ),C(G,H <sub>0</sub> )CN (n-C,H <sub>0</sub> ),C(G,H <sub>0</sub> )CN CH O,CH O,CH O,CH	1 2 9 2	NaNH <sub>2</sub> NaNH <sub>2</sub> NaNH <sub>2</sub>	Ether Ether Toluene	350 560 1015
	C2115C(C112)21C(C413)CN [C215C(C12)2]2C(C415)CN i-C,H,CH(C,H,)CN	54 70-80	NaNH <sub>2</sub> NaNH <sub>3</sub>	Tolucne Ether	500 1031, 1034,
	(i-C, H,)2C(C, H,)CN	02	NaNH2	Toluene	1030
	$[\mathrm{CH}_2 = \mathrm{CHO}(\mathrm{CH}_2)_2]_2 \mathrm{C}(\mathrm{C}_6\mathrm{H}_5) \mathrm{CN}$	20	NaNH2	$C_{f g}H_{f g}$	1038, 1040
	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN	<b>80-</b> 00	80-00 NaNH2	$\mathtt{C}_{\mathfrak{b}}\mathtt{H}_{\mathfrak{g}}$	178, 254, 1041, 1049
	1-Phenyl-2-ethyleyelopropane- 1-carbonitrile	40	NaNH2	Ether	258
	α-Phenyl-β-lsopropylaerylo- nltrile	38	NaNH <sub>2</sub>	Ether	258
	1.Phenyleyelopentane. 1.earbonitrile	40	$NaNH_2$	Ether	300
	4-Phenyltetrahydropyran- 4-carbonitrile	40	NaNH <sub>2</sub>	Toluene	77, 499
	4.Phenyltetrahydrothiapyran. 4-earbonitrile	47	$NaNH_2$	Toluene	77, 409
	4-Phenylppcridine- 4-carbonitrile	Poor	$NaNH_2$	Tolucne	505
	n-C <sub>5</sub> H <sub>11</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN	i	NaOH	None	279
	"-Cshilch(Csh.)CN CH2[OCH2CH2CH(Csh.)CN];	1 %	Na NaNH,	Liquid NH <sub>3</sub> Toluene	1025
	1-Phenyleyelohexane- 1-carbonitrile	28	NaNH2	Ether	307, 300
	1-Methyl-4-phenylpiperidine- 4-carbonitrile	00	NaNH2	Toluene	77, 503, 505

Note: References 577-1080 are on pp. 322-331.
• The halogen was not specified.

### ORGANIC REACTIONS

TABLE XIV—Continued

Refer-	ence	1043	1044		77	188	178.77	1041	1045	171, 1016	576	102	254		279 1047	505	•	203	
	Snivent	Ether	Toluene	organio T	Nane	None	Ether	$C_6H_6$ Tolueno	Ether	СоПе	Tnluene	Toluene	Tolucne		None		Tnlueno	Toluene	
)CN		Base NaNH,	NaNH <sub>2</sub>	NaNH2	TOH	NaOH	NaNH2 NaNH3		Nan II. Nan II.	NaNII2	NoN 1	NoNE,			NaOII	. Nan 112	NaNH <sub>2</sub>	41 KNH <sub>2</sub>	
MONONITRILES, RCH(R')CN	Yield,	Product	(α-Cyclopentyl)phenyl- acetanitrile 70	Phenyl-(2-pyrldyl)acctualtrilc Phenyl-(4-pyrldyl)acctualtrilc		n.C,H <sub>13</sub> CH(C,H <sub>5</sub> )CN	7-C <sub>0</sub> H <sub>13</sub> CH(C <sub>0</sub> H <sub>2</sub> CH(C <sub>0</sub> H <sub>2</sub> )CN 38 (C <sub>0</sub> H <sub>2</sub> O) <sub>2</sub> CHCH <sub>2</sub> CH(C <sub>0</sub> H <sub>2</sub> O) <sub>2</sub> CH(C <sub>0</sub>	2,H <sub>2</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN (CH <sub>2</sub> ) <sub>2</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN 80-90	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN	(a-Cyclohexyl)phenyl- acetonitrilo	ĕ			Phenyt-(3-methyr-2-pyres-7) acetonitrile	LCH.CH(C,Hz)GN	C2H5O2CCH(C3H7·t)-	CH(C <sub>6</sub> L <sub>6</sub> )C <sub>1</sub> N 1,3,5-Trimethyl-		4-phenylplpcridine- 4-carbonitrilo
MOAN .	ALKYLATION	Alexisting Agent	<sub>ق</sub>	2-Chloropyrldine P		n C.H.Br		(C <sub>2</sub> H <sub>2</sub> O <sub>3</sub> CH <sub>2</sub> O <sub>3</sub>		ē	Cyclohexyl bromide (	Cyclohexyl bromlde (	mide	2-Bromo-3-methyl- pyridine		n-C,H <sub>16</sub> 1 i-C,H,CHBrCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	•	TO TO TO TO	CH <sub>3</sub> N(CH <sub>2</sub> CHCCC <sub>3</sub> )?

R' C<sub>6</sub>H<sub>6</sub> (Cont.)

	11113	AU.	XII	MIL	14 0	1, 13011	2101	, ,,,,					
34 84 84 34 34 34, 1001, 1048	34 34 566	195	7. 7.	564	270 195	300		1049 1037	178 178	178	188	503, 505	503, 505
None (C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N-H <sub>2</sub> O (i-C <sub>3</sub> H <sub>7</sub> ) <sub>2</sub> NC <sub>2</sub> H <sub>5</sub> -H <sub>2</sub> O CH <sub>3</sub> OH Ethanol	n-C,H,OH n-C,H <sub>11</sub> OH Ether	Liquíd-NH3-ether	Ethanol Ethanol	None	None Llquld NH3-ether	Bther		Ether Toluene	°н° С°н°	$C_6H_6$	Ether	Toluene	Toluene
$N_{10}OH$ $N_{10}OH$ $N_{10}OH$ $N_{10}OCH_{1}$ $N_{10}OC_{2}H_{5}$	NaOC <sub>3</sub> H <sub>7</sub> -n NaOC <sub>5</sub> H <sub>11</sub> -n NaNH,	NaNII.	NaOC <sub>2</sub> H <sub>5</sub> NaOC <sub>2</sub> H <sub>5</sub>	NaOH	NaOH KNH2	NaNH2		NaNH <sub>2</sub> NaNH <sub>2</sub>	$N_{2}N_{2}$ $N_{2}N_{3}$	$_{ m NaNH}_{ m 2}$	NaNH <sub>2</sub>	$NaNH_2$	$_{ m NaNH_2}$
55 50 13 33	28 Poor 34	33	11	1	18	œ		88	76 100	00	99	19	90
Conf.CH.CH.CH.ON Conf.CH.CH.Ch.ON Nono Conf.CH.Conf.Conf.Conf.Conf.Conf.Conf.Conf.Conf	C <sub>6</sub> II, CH <sub>2</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN C <sub>6</sub> H <sub>5</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN CH-CH-CH-CH-CN	C4H,CH,CH(C4H,)CN (C4H,CH,CHC,H,)CN	C <sub>6</sub> H <sub>s</sub> CH <sub>2</sub> CH(C <sub>6</sub> H <sub>6</sub> )CN C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH(C <sub>6</sub> H <sub>5</sub> )CN	C <sub>6</sub> H <sub>5</sub> CH=C(C <sub>6</sub> H <sub>6</sub> )CN	$n \cdot C_6 H_{17} CH(G_6 H_5) CN$ $C_6 H_6 CH(CH_3) CH(C_6 H_5) CN$	CGE, CGE, CON		C <sub>6</sub> H <sub>5</sub> O(CH <sub>2</sub> ),CH(C <sub>6</sub> H <sub>5</sub> )CN CH <sub>2</sub> [O(CH <sub>2</sub> ),CH(C <sub>6</sub> H <sub>5</sub> )CN] <sub>2</sub>	Phenyl-(4-quinolyl)acetonitrile Phenyl-(5-chloro-4-quinolyl)-	Phenyl-(7-chloro-4-quinolyl)- acetonitrile	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N(CH <sub>2</sub> )(CH <sub>2</sub> ) <sub>2</sub> Cl C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N(CH <sub>2</sub> )(CH <sub>2</sub> ) <sub>2</sub> - CH(C,H <sub>1</sub> )CN	1.Cyclohexyl-4-phenyl- plperidinc-4-carbonitrile	1,4-Diphenylpiperidine- 4-carbonitrile
C,H,CH,CH,CI C,H,CH,CI C,H,CH,CI C,H,CH,CI C,H,CH,CI C,H,CH,CI	Canson Ca	C <sub>4</sub> H <sub>5</sub> CH <sub>2</sub> Cl	$C_6H_5CH_2Br$ $C_6H_5CH_2I$	C,H,CHCl2 C,	$n \cdot \mathbf{c}_{\mathbf{c}} \mathbf{H}_{17\mathbf{I}}$ $\mathbf{c}_{\mathbf{c}} \mathbf{e}_{\mathbf{d}} \mathbf{G} \mathbf{H}_{\mathbf{c}} \mathbf{G} \mathbf{H}_{\mathbf{c}}$	CH <sub>2</sub> Br	్రి	C <sub>4</sub> H <sub>5</sub> O(CH <sub>2</sub> ) <sub>3</sub> Dr CH <sub>2</sub> [O(CH <sub>2</sub> ) <sub>4</sub> CI) <sub>2</sub>	4.5-Dichloroquinoline 4,5-Dichloroqulnollne	4,7-Dichloroquinoline	$C_6H_5CH_2N(CH_3)(CH_2)_2($	$cyclo-\\ C_6H_{11}N(CH_2CH_2CI)_2$	C <sub>6</sub> H <sub>5</sub> N(CH <sub>2</sub> CH <sub>2</sub> Cl) <sub>2</sub>

Note: References 577-1080 are on pp. 322-331.

ntinued	BCH(R')CN	
" A DI E XIV—Continued	TABLE	

	Refer-	ence		505, 77, 503	1037	11				195	r c	Ť S	155	254	•	1042.	1042,	1042.	1041	1015	254	1038	190		
		Solvent		Toluene	1	Toluene				Liquid NH3-ether	C.11s	Tolucne	ì	Tolugue	oranni	Toluene	CeIIs	с.п.	9 10 10 10	Total	and the second	Tolueno Tolueno	1	Toluene	
25		Thear	Disso	No.NII.			Nan II.			1	KNH,	Now H2	Navius.	NaNH2	NaN112	NaN II.	No.NII.		NaNH2		NaNH2		NaNII2	NaNII2	
7,07,	4	Yield,	%	ŕ	3	l	37				6	82	<u>-1</u>	99	13	2	, ,	ŝ	43		93	13	I	1	
TABLE XIV—Continued	Mononitrices, RCH(E)	י בי בי אינו	Product		1-Benzyl-4-phenylpheridine-	Z	p-CH3C6H4SO2N	CH2 CH2	ch, ch,	H. OKONO. H.	NOCH OTHER	ND(0-10"11"C)1(C"11"C)-0)CN	Chlorophenyl-(2-pyridyl)-	acetonitrile	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> CH(C <sub>6</sub> H <sub>4</sub> CH))-	p-Chloropneny I.C. 17 acetonitrile	$(C_2\Pi_5)_2N(C\Pi_2)_2^{-1}$ $CH(C_6\Pi_4Cl-p)CN$	(C2115)2N(CH2)3-	CH(Centor-Dec	CH(C <sub>6</sub> H <sub>3</sub> Cl <sub>2</sub> -3.4)CN	NCH, C(C, H,-n), CN	CHOCH.C.H.)CN	(CH <sub>3</sub> )2N(CH <sub>2</sub> )2]2- [CH <sub>2</sub> =CHO(CH <sub>2</sub> )2]2-	C(Ce,II,CH3-0)CN	1-Methyl-4-(2 -meenon) phoeridine-4-carbonitrile
		ALKYLATI		Alkylating Agent	C <sub>11</sub> -C <sub>13</sub> C, H, CH <sub>2</sub> N(CH <sub>2</sub> CH <sub>2</sub> Cl) <sub>2</sub>	and imidopropyl	bromide	N(CH2CH2CI)2				C.H.),CHCl	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl	2-Bromopyridine	CH.), N(CH.), Cl	2-Bromopyridine	$(C_2H_5)_2N(CH_2)_2^{Cl}$	(C.H.),N(CH2),Cl	7,072	$(C_2H_5)_2N(CH_2)_2Cl$	1	n-C4H9Br	(CH <sub>2</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl	CH2=CHO(CH2)2C-	CII3N(CH2CH2CI)2
				<b>1</b> 4	C,H5 (Cont.)								A.CIC.H.			$p ext{-CIC}_{\mathbf{c}}^{\mathbf{H}}$				3,4-Dichlorophenyl (C2H5)2N(CII2)2Cl	(	\ NCH2	C, H, CH,	O-CH3C,H4	O-CH,OC,H,

			A second	7	NoNO	Ħ o	1007	
		Cyclohexyl bromido	Cyclonexy(o-mechoxyphenyl)- acctonitrilo	3	200	979	1008	
п	$m\text{-}\mathrm{CH}_3\mathrm{OC}_6\mathrm{II}_4$	CII3N(CII2CII2CI)2	I-Methyl-4-(3'-methoxyphenyl)-	I	1	ı	501	
11	$p ext{-} ext{CII}_3 ext{C}_6 ext{II}_4$	$(\mathrm{CH_3})_2\mathrm{N}(\mathrm{CH_2})_2\mathrm{Cl}$	$(CH_3)_2N(CH_2)_2$ - $CH(C_3H_3CH_2-9)CN$	43	$NaNH_2$	$C_6H_6$	254	
11	$p ext{-}\mathrm{CH}_3\mathrm{OC}_6\mathrm{H}_4$	$\mathrm{CH_3N}(\mathrm{CH_2CH_2CI})_2$	1-Methyl-4-(4'-methoxyphenyl)-	63	$NaNH_2$	Toluene	503, 505	1.
		$(C_2\Pi_5)_2N(C\Pi_2)_2Cl$	$(C_2H_5)_2N(CH_2)_2$ - $CH(C_4H_1OCH_2)_2$ -	20	$NaNII_2$	$C_{\mathbf{G}}\mathbf{H}_{\mathbf{g}}$	1042, 1041	تننن
11	2-Methoxy-5-	$n\text{-}\mathrm{C}_3\Pi_7\mathrm{Br}$	n-C <sub>3</sub> H <sub>7</sub> - CHC, H-(OCH-)/CH-)-2 51CN	92	$NaNH_2$	Сен	1007,	ΑШ
	if in the state of	$(C_2\Pi_5)_2N(C\Pi_2)_2Cl$	$(C_2H_5)_2N(OH_2)_2$ $C_{THC}$ II (OCH )(CH >-9 51CN	83	NaNH <sub>2</sub>	$C_6H_8$	1007,	717
11	3,4-Dimethoxy- phenyl	$\mathrm{CH_3N(CH_2CH_2CI)_2}$	1-Methyl-4-(3',4'-dimethoxy-phenyl)pleridine-4-	1	$NaNH_2$	Toluene	190	MIIO
11	n-C,111,9	n·C <sub>8</sub> H <sub>1</sub> ·Br	n-C <sub>3</sub> H <sub>19</sub> CII(C <sub>8</sub> H <sub>17</sub> - $n$ )CN	25	NaNH,	C,H,	289	ΤΛ
11	a-Naphthyl	$(CII_3)_2N(CH_2)_2CI$	$(CH_3)_2 N(CH_2)_2 CH(C_{10}H_7-\alpha)CN$	22	NaNH2	CaH	254	O1
		CII3N(CII2CII2CI)2	1-Methyl-4-(a-naphthyl).	20	NaNH2	Toluene	503	3 E
		2.Chloropyridine	Proceedings 2-Caraching 2-Pyridyl-(α-naphthyl)-	1	$NaNH_2$	Toluene	1044	POTT
н	o-Benzyloxyphenyl	CH3N(CH2CH2CI)2	I-Methyl-4-(o-benzyloxy- phenyl)plperidine-	1	$NaNH_2$	Tolucne	190	. מתני
и	n-C11.	CII.1	4-earbonitrile	ç				Au
CI13	CH3	CII,0(CII,),Br	CH-O(CH-)-CCH-) CN	8 1	LIN(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	Ether	65	U
	•	CH2=CHCH2CH	CH3 = CHCII, C(CH2), CN	<b>5</b> 5	TANH.	Cette Telber	53, 122	TA
		CII, = CHCH, CI		Good	NaNH,	None	199	TT
		$CII_2 = CIICII_2CI$	CH2=CHCH2C(CH3)2CN	1	NaNII	Inert solvent	1013	IV.
		CH2 = CHCH2CI	$CH_2 = CHCH_2C(CH_3)_2CN$	83	NaN(C2H5)2	Ether	53	ليلا
		Cl(CII,),Br	CHOIL COLORS	19	BrMgN(C2H5)2	Ether	53	COL
		Censcii ci	None	1	NaNH2	C <sub>6</sub> H <sub>6</sub>	122	
		Cells CH2CI		ا و	NaUC2H5 NaH	Ethanol	1017	
$C_k\Pi_k$	$c_2 \pi_s$	$\mathbf{c_{a}u_{s}c_{II_{2}CI}}$ $\mathbf{c_{z}H_{s}Br}$		20	LIN(C2H5)2	Ether	255	
Note: References 577	71080 are on r	100 000 00		7	77.77	Ether	1050	J

te: References 577-1080 are on pp. 322-331.

### ORGANIC REACTIONS

					· ·	)IVG2	11111	_														
	reler- ence		255	255	53 90	53, 122, 1013	1050	1050	1021	53 1013	53, 122	1030	65	E1 3	53, 122,	1050	S 8	1000	8	1050	255	S
		Solvent	Ether	Effice	Ether	rii"o	Ether	Ether	C.H.	Ether		n'o	Lither	Calla	C.III.	c.n.	C.II.	Calla	Inert solvent Calla-ligroin	Inert solvent	Inert solvent	C <sub>e</sub> H <sub>e</sub>
75	, tol	l, Base		-,	LIN TINICAL.	8	NaN(C, Hs)2		4 <b>1</b> 4	Cu Cu InMaX(C <sub>4</sub> 11 <sub>11</sub> )2		78 XaXII.	: ::::::::::::::::::::::::::::::::::::	NaNII,	Navila Navila			73 ANGELIS		88 NaCells Bryan(Celln)2		70 NaCells
ed	KCH(1	Xieio Xieio	2	1	81	91.63	80	; <b>!</b>	1 1	1 6	- 00	•		•	, •	r						)c.y
TABLE XIV—Continued	ATTACHON OF MONONITRIES, RCH(19/104)		Product	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> CCN	$\mathrm{CH}_2 = \mathrm{CHCH}_2\mathrm{C}(\mathrm{C}_2\mathrm{H}_5)_2\mathrm{CN}$	$CH_2 = CHCH_2C(C_2H_5)_2CN$ $CH_2 = CHCH_2C(C_2H_5)_2CN$	CII; = CHCII; C(C; II;); C:	CH3 == CHCH4C(C; 115);CN	CH; = CHCH; C(C, H5); CN	$CII_2 = CIICII_2 C(C_2II_5)_2 CN$ $CII_4 = CIICII_2 C(C_2II_5)_2 CN$	CII; = CIICII; C(C; II;); CN	CH2 CHCC4113.CN	(C,115), V(CH,2), C(C,115), CN	Constant Constant	C, 11, C11, C(C, 11, 1), CN	(i-c,ii-),c(c,ii,)c.N	Allyf.z-leopropylbutyronltrife	$(CH_2 = CHCH_2)_2(C_2H_3)CN$	2-Allyf-z-etflyfcapromittile	(CII = CIICII ), CCN	$(CH_2 = CHCH_2)_2CCN$	$(CH_2 = CHCH_2)_2CC_3$ $(CH_3 = CHCH_2)_2C(C_3H_{22}^{-1})CN$
	ATVITA	ALALA	Alkylating Agent	(C2H3)2SO4	CH2=CHCH2CI	CII, = CHCH; Cl	CIL = CHCH CI	CH.=CHCH!CH	CH; = CHCH; Br	CH; CHICH IN	CH, = ChCH, Br	CH;=CHCH;I	n.C.H.Br	C, II, CH CI	C, II, CH, CI	C. 115C112C1		CII, = CHCH, Br	CH; = CHCH;CI	Canst CHCH.Cl	CH, = CHCH, CI	CH2 = CHCH210 CH2 = CHCH210 . CH
			ž	C.H. (Cont.)	a a											‡	1.0,117			CH;=CHCH;		
				r t	$C_2H_5$												C <sub>2</sub> H <sub>3</sub>		C,H,S	Cins CH = CHCH	•	

					****			٠.		,11110	111,12	-1	~	,
122	359 1023, 501	583	34	1032	1032, 359	1043	1044	190	305	1018 254	359 1035 1053	279 254	359	
$C_{f d}\Pi_{f d}$	$C_{oldsymbol{d}}\mathbf{H}_{oldsymbol{d}}$ Toluene	Ether	Ethanol	Ether	C <sub>6</sub> H <sub>6</sub>	Ether	Toluene	Toluene	Llquid $\mathrm{NH_3}$	Ether Toluene	C <sub>o</sub> H <sub>6</sub> Ether C <sub>o</sub> H <sub>6</sub>	None Toluene	С,Н	
Good NaNH2	$N_{1}N_{1}$ $N_{2}N_{1}$	$NaNH_2$	NaOC <sub>2</sub> H <sub>S</sub>	Na	NaNII2	$NaNH_2$	$NaNH_2$	NaNH2	NaNII2	$NaNH_2$ $NaNH_2$	NaNH2 NaNH2 NaNH2	$NaOH$ $NaNH_2$	NaNH2	
G00C	20	15	1	5	53	i	1	67	73	1 8	25 35	38	1	
(CN)CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	$C(C(H_2)_2C(C(H_3))(C_6H_5)CN)$ $C(H_3)_2N(C(H_2)_2$ $C(C(H_3)_2N(C(H_2)_2)$	C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH(CH <sub>3</sub> )- C(CH <sub>3</sub> )(C <sub>6</sub> H <sub>5</sub> )CN	Coll, Cli, C(CH, )(Coll, )CN	C4115C(C2115)2CN	$C_0H_3$ C( $C_2H_3$ )( $C_0H_6$ )CN	a-Phenyl-a-eyelopentyl- butvronitrile	$\alpha$ -Ethyl- $\alpha$ -phenyl- $\alpha$ -(2-pyridyl)- acetonitrile	$(C_2H_5)_2N(CH_2)_2$ - $C(C_5H_5)(C_6H_5)CN$	1-Phenyleyclopropane- 1-carbonitrile	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C(CH <sub>3</sub> )(C <sub>2</sub> H <sub>5</sub> )CN (CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> * C(C <sub>4</sub> H <sub>3</sub> S)(C <sub>5</sub> H <sub>4</sub> N·2)CN	Cl(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>3</sub> )(C <sub>2</sub> H <sub>7</sub> ·n)CN i·C <sub>4</sub> H <sub>5</sub> C(C <sub>6</sub> H <sub>5</sub> )(C <sub>5</sub> H <sub>7</sub> ·n)CN C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> · CC <sub>4</sub> H <sub>7</sub> ·n/C H <sub>7</sub> ·n/C	$C_6\Pi_5 C\Pi_2 C(C_6\Pi_5)(C_3\Pi_7 - n) CN$ $(C\Pi_5)_2 N(C\Pi_2)_2  C(C_5\Pi_4 N - 2)(C_6\Pi_4 N - 3) CN$	$\mathrm{Cl}(\mathrm{CH_2})_2\mathrm{C}(\mathrm{C_0H_5})(\mathrm{C_4H_9-n})\mathrm{CN}$	
$C_6\Pi_5\Pi_2$ CI	$\mathrm{Cl}(\mathrm{ClI}_2)_2^{\mathrm{Cl}}$ $(\mathrm{ClI}_3)_2^{\mathrm{N}}(\mathrm{ClI}_2)_2^{\mathrm{Cl}}$	$\mathrm{CH_3CHBrCO_2C_2H_5}$	CollsCII2CI	C <sub>2</sub> H <sub>3</sub> I	$C_2^{-1}$ $C_3^{-1}$	Cyclopentyl bromide	2.Chloropyridino	$(C_2\Pi_5)_2N(C\Pi_2)_2CI$	None	C11 <sub>3</sub> 1 2-Yromopyrldine	CI(CIT <sub>2</sub> ) <sub>2</sub> CI i-C <sub>1</sub> IT <sub>2</sub> Br Br(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	C <sub>o</sub> li <sub>s</sub> CH <sub>2</sub> Ci 2-Bromopyridine	$\mathrm{Cl}(\mathrm{CH}_2)_{\underline{a}}\mathrm{Cl}$	on pp. 322-331. CN
	$C_{\delta}\Pi_{\delta}$			Cells					C <sub>6</sub> 11 <sub>s</sub>	Collscii2	C <sub>6</sub> II <sub>5</sub>		Cells	Note: References 577-1080 are on pp. 322-331.  The nittile alkylated was Cri
<b>←</b>	cu,			C2115					CI(CIII <sub>2</sub> ) <sub>3</sub>	(' <sub>1</sub> 11 <sub>5</sub> (CU <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub>	n.C <sub>3</sub> II <sub>7</sub>	(CII <sub>3</sub> ) <sub>2</sub> N(CII <sub>3</sub> ) <sub>2</sub>	n-C,II,	Note: Refer † The nitelle

non-	RCH(R')CN
XIV-Continue	5
TABLE XIV	

Refer-	enco	101	191	101	161	161	191	254	954		254	254	954	}	178	C I	7.18	178		254	1003	2701	
	Solvent	C.II.	3	$C_6H_6$	$C_6\Pi_6$	$C_6\Pi_6$	CoH	molnene	Tono	Toluene	Tolucne	Toluene		Toluene	ţ	Cene	CoH	ì	$c_{ m eH_6}$	onout-m	TORON	Toluene	
CN		Base	NaNH2	NaNII2	NaNH2	NaNIIa	1	Nan na	$NaNH_2$	NaNHa	NaNHa	History	Nanaz	NaNII2		$NaNH_2$	$NaNH_2$		NaNH2		NaNH2	NaNH2	
H(R')	Vield.	%	89	81	20			22	20	78	2	2	85	74		88	86		95		67	90	
RC RC RC	ALKYLATION OF MONUMITED.	fortherin	Toungal Ash	(CII <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>1</sub> CO (CII <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>1</sub> CO (CII <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> )N(CH <sub>2</sub> ) <sub>2</sub> N(CH <sub>2</sub> )N(CH <sub>2</sub> ) <sub>2</sub> N(CH <sub>2</sub> )N(CH <sub>2</sub> N(CH <sub>2</sub> )N(CH <sub>2</sub> )N(CH <sub>2</sub> N(CH <sub>2</sub> )N(CH <sub>2</sub> )N(CH <sub>2</sub> )N(CH <sub>2</sub> N(CH <sub>2</sub> )N(CH <sub>2</sub> )N(CH <sub></sub>	(C2U5)2N(CH2)2- C(C4U5)(C4H9-1)CN	α-(i-Butyl)-α-phenyl-γ-(1-	8	t	(1-plperidyl)butyronitrilo	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> - C(C <sub>6</sub> H <sub>11</sub> -cyclo)(C <sub>6</sub> H <sub>4</sub> N-2)CN	(CII3)2N(CII2)2- C(C, II, N-2)(C, H3)CN	(CH <sub>2</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> .	C(C, H 2N-1) C(C, H 2N-1)	C(C <sub>6</sub> H <sub>5</sub> )(C <sub>6</sub> H <sub>11</sub> -cyclo)CN C(C <sub>6</sub> H <sub>5</sub> )(C <sub>6</sub> H <sub>11</sub> -cyclo)CN	a.Phenyl-a-(dimethylamino)-	butyronitrile	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> ; C(C <sub>6</sub> H <sub>5</sub> )(C <sub>9</sub> H <sub>6</sub> N-4)CN	a-Phenyl-a-(5-chiotor-r- quinolyl)-y-(dimethylamino)-	butyronitrile	quinolyl)-y-(dimethylamlno)-	butyronitrile	C(C,H,N-2)(C,H,CI-p)CN	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> - C(C <sub>4</sub> H <sub>3</sub> S)(C <sub>6</sub> H <sub>11</sub> -cyclo)CN
-	ALKYLATIO		Alkylating Agent	(CII,)2N(CII,)2CI-IICI	$(C_2H_5)_2N(CH_2)_2Cl_0HCl$	6-(1-Piperidyl)ethyl	ehloride hydroehloride	chloride hydrochloride	β-(1-Piperidyl)ethyl	2.Bromopyridine		4. Bromopyridine	4-Diomoral	Cyclo-CeII11Br	2-Bromo-6-methyl-	pyridine	4-Chloroquinollne	4,5.Dleliloroquinoline		4,7.Diehloroquinoline		2-Bromopyridine	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl
				, r,	C <sub>6</sub> 115			Сейь	C.II.	Control H.		$C_6H_5$										$p ext{-ClC}_6^{ ext{II}_4}$	Cyclo-CeII 11
				11	i.C.IIs			(CIL),C=CII	TOV WOLL	CII <sub>2</sub> =C(CII <sub>2</sub> )OII <sup>2</sup> %		$(C1I_2)_2N(C1I_2)_2$										CH ) N(CH,), p-CIC,H4	

S

		THI	<b>E A</b> :	LKY	/LATI	ON OF	ES'	TER	s Al	ΝD	NIT	CRII	LES	;
254	289 1007, 1008	254	254	254	279 191	1043 1044 254	254	254	254	254	254	77, 191	279 1007	178
Toluene	$\begin{array}{c} \text{Toluene} \\ \text{G}_6 \text{H}_6 \end{array}$	Toluene	Toluene	Toluene	$N$ one $C_6H_6$	Ether Toluene Toluene	Tolucne	Tolucne	Toluene	Toluene	Toluene	Toluene	None Ether	$c_{\mathbf{g}}\mathbf{H}_{\mathbf{g}}$
NaNII	$NaNH_2$ $NaNH_2$	$MaNH_2$	$NaNH_2$	$_2$ NaNH $_2$	$NaOH$ $NaNH_2$	NaNH <sub>2</sub> NaNH <sub>2</sub> NaNH <sub>2</sub>	$_{\rm NaNH_2}$	NaNH2	NaNH <sub>2</sub>	NaNH <sub>2</sub>	NaNH <sub>2</sub>	$NaNH_2$	$NaOH$ $NaNH_2$	$NaNII_2$
78	7.0	41	44	80	18	187	83	93	89	33	46	72	11	97
(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>3</sub> H <sub>4</sub> N-2) <sub>2</sub> CN	(n-C <sub>10</sub> II <sub>21</sub> ) <sub>2</sub> C(CII <sub>3</sub> )CN α-(2-Diethylaminoethyl)· α-(2-methoxy-	5-methylphenyl)valeronitrile $(CH_2)_2N(CH_2)_2$	(CH3)2N(CH3)2- (CH3)2N(CH3)2- CO H CH 2N H M M	(CII <sub>3</sub> ) <sub>2</sub> N(CII <sub>3</sub> ) <sub>2</sub> .	C(c <sub>1</sub> 1,0C(1 <sub>2</sub> 7))C <sub>3</sub> 11,1 <sup>3</sup> 12,CN C <sub>3</sub> 11 <sub>5</sub> CH <sub>2</sub> C(c <sub>3</sub> 11 <sub>5</sub> )C <sub>3</sub> 11 <sub>11</sub> -n)CN (C(1 <sub>3</sub> ) <sub>2</sub> N(C(1 <sub>3</sub> ) <sub>2</sub> -	C(ef15,C3119,C31 C <sub>6</sub> H c(C <sub>6</sub> H 5,C31 C <sub>6</sub> H 5,C31 C <sub>6</sub> H c(C <sub>6</sub> H 5,C31 C <sub>6</sub> H 5,C31 C <sub>6</sub> H c(C <sub>6</sub> H 5,C31 C <sub>6</sub> H 5,C31 C <sub>6</sub> H c(C <sub>6</sub> H 5,C31 C <sub>6</sub> H	$C(C_6\Pi_5)(C_5H_4N-2)CN$ $(CH_3)_2N(CH_2)_3$ -	$C(C_6H_2)(C_5H_4M^2)CN$ $(C_2H_5)_2N(CH_2)_2$ - $C(C_1H_2)_2N(CH_2)_2$ -	<pre>c(c<sub>6</sub>11<sub>8</sub>(C<sub>6</sub>11<sub>4</sub>11·2)C<sub>1</sub>N &lt;-Phenyl-α-(2-pyridyl)-γ- (1'-plperidyl)butyronitrile</pre>	(CII <sub>3</sub> ) <sub>2</sub> N(CII <sub>2</sub> ) <sub>2</sub> - C(C <sub>6</sub> II,Cl-0)(C <sub>5</sub> II,N-2)CN	(CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> . C(CH, C.H.)(C.H. N.9)CN	(C <sub>2</sub> H <sub>2</sub> ) <sup>2</sup> N(CH <sub>2</sub> ) <sup>2</sup> - C(C <sub>4</sub> H <sub>2</sub> )CN(CH <sub>2</sub> ) <sup>2</sup> - C(C <sub>4</sub> H <sub>2</sub> )CN	None 7-13 7-13 7-13 7-14 None 7-19 13 14 15 15 15 15 15 15 15 15 15 15 15 15 15	phenylbutyronitrie (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> - C(C <sub>6</sub> H <sub>5</sub> )(C <sub>9</sub> H <sub>6</sub> N-4)CN
$(GII_3)_2 N(CH_2)_2 Cl$	$^{n-C_{10}II_{21}Br}$ $(C_{2}II_{5})_{2}N(CII_{2})_{3}CI$	2-Bromopyrldine	2-Bromopyridine	2-Bromopyridine	$C_qH_sCH_s$ CI (CH $_2$ ) $_2$ CI-IICI	Cyclopentyl bromide C <sub>2</sub> 11 <sub>5</sub> Br (CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl	$(CH_3)_2N(CH_2)_3CI$	$(C_2 \Pi_5)_2 N (C \Pi_2)_2 C I$	\$\theta \cdot \text{Plperidyl} \text{ethyl} \cdot \text{chloride}	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>3</sub> ) <sub>2</sub> CI	(CII <sub>3</sub> ) <sub>2</sub> NCII <sub>2</sub> Cl	$(C_2\Pi_5)_2N(C\Pi_2)_2CI$	C,115Cll2Cl Cyclohexene oxide	4-Chloroquinoline
	n-C <sub>10</sub> H <sub>21</sub> 2-Methoxy- 5-methylphenyl	C411,CIT,	p-CII3C4II4	p-c1130C4114	C4115 C4116	C,11s			4 55	0-515,114	C4115C112	ر 113	C <sub>6</sub> III <sub>5</sub>	4-Chloroqu
	CU <sub>3</sub> n-C <sub>3</sub> U <sub>7</sub>	$(C11_3)_2N(C11_2)_2$	$(\mathrm{CH}_3)_2\mathrm{N}(\mathrm{CH}_2)_2$	(CII <sub>3</sub> ) <sub>2</sub> X(CII <sub>2</sub> ) <sub>2</sub>	$n$ - $C_{s}H_{11}$ cyclo- $C_{s}\Pi_{s}$	2-Pyridyl			o. Deethal	101110	z-Pyridyl	n-C <sub>4</sub> II <sub>13</sub>	(C <sub>1</sub> II <sub>2</sub> ) <sub>1</sub> N(CII <sub>2</sub> ) <sub>2</sub>	Nide: Hefere

Net: References 577-1030 are on pp. 322-331.

(C2H<sub>2</sub>)<sub>2</sub>NCH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>-CH<sub>2</sub>Cl 6-(4-Morpholinyl)butyl

5	3
tea.	
Continu	
XIV	
TABLE XIV—Continued	

,	Refer-	enec	1/0	178		1054		1004	171	101, 1002	1055		1055	2001	1043		191, 1055		191	, ,	1055	191		1055			1055		gent	1055			
		Solvent	C, H,	5	CeHs	146	Emer	C.H.	Liquid Nifa	Calle	•	CeIIs		$C_6H_6$		Ether		CeIIs	C.H.		Сене	•	$c_{\rm eH_s}$	1	รับ เล		, H.	200	C,H		CeHe		
Nova		pla	%. Base	98 NaNH2	- Now	91 Names	NaNH2		94 NaNH2	•	72 NaN 112	# X - 1	- Nanuz	TW.Y	- Nan 112	No.N.H.	2	82 NaNH2		90 NaNH <sub>2</sub>	;	Nan 12	No.N. No.	25 Mary 28	NaNH,			- NaNH2		- Naming	NaNII,		
TABLE XIV—Continued	OF MONONITRILES, KCHI	ALKYLATION OF MALE YIELD					•	C.H.C(CH <sub>3</sub> )(C <sub>6</sub> H <sub>11</sub> )CN				CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> .		(CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> Ch(CH <sub>3</sub> )			henyl-			C(C, 11, )(C, 11, 1) C.	α-Cyclohexyl-α-pnenyr-7	(I-pyrionaly)	COLUMN TO THE TOTAL OF THE TOTA	Cyclobexyl-a-phenyl-7	(1-piperldyl)butyronitrlle	(C,H,),NCH(C,H,)CH2-	C(C, H, )(C, H, 1, )CN	CHOILE CHOIL	CG.H.)CN	-(1-cheryl-(4-morphollny1)-	butyflphenylacetonitrile	(C,Hs)2NCH2C(CH3)2-	CIT TO CONTRACT OF THE CONTRAC
TA		ALKYLATION		tallng Agent	lne		4,7.Dichloroquinoline		CII,X†			, recalling North, clinical		CH.), NCH, CH(CH <sub>3</sub> )Br (		(CH <sub>3</sub> ),NCH(CH <sub>3</sub> )CH <sub>2</sub> Br (		Cyclopentyl bromide	) 13(1-13°CH-1),C1-111C1			ide			p.(1-Piperidyi)cunyi	chloride hydrocinoling (C.H.)2NCH(C.H.5)CH2	(C2H6)2NCH(C2H5/CH2C)	(	NCH2CH(CH3)CI		5-(4-Morphollnyl)butyl	chloride (C,H,),NCH,C(CH3)2-	D'HO
					ъ,	r,, C,IIs (Cont.)			<b>P</b>	91780																							

Cyclohexyl  $(=C_6\Pi_{11})$ 

1055	1056	264	1004 1057	1057, 91 25	25	25		27 27	25, 329 27 25	1057 27		329	
$C_6H_6$	Toluene	Ethanol	C <sub>6</sub> H <sub>6</sub> C <sub>6</sub> H <sub>6</sub>	$C_6H_6$ Ethanol	$C_6H_6$	$C_dH_g$		Xylene-(•C4H,0H Xylene	C <sub>6</sub> H <sub>6</sub> Xylenc-t-C <sub>4</sub> H <sub>9</sub> OH C <sub>6</sub> H <sub>6</sub>	CoH CoH		СДН	
$NaNH_2$	$_{ m NaNH}_{ m z}$	$\rm NaOC_2H_5$	$NaNH_2$ $NaNH_2$	$ m NaNH_2$ $ m NaOC_2H_5$	$ m Na0C_2H_5$	NaNII2		KOC4H9-1 KOC4H9-1	NaNH <sub>2</sub> KOC <sub>4</sub> H <sub>9</sub> -t NaNH <sub>2</sub>	NaNH <sub>2</sub> KOC <sub>4</sub> H <sub>9</sub> -t		NaNH <sub>2</sub>	
1	81	100	88 70	14-80	25	57		88 72	94 72 47	52		80	
$(n\text{-}\mathrm{C_4H_9})_2\mathrm{N}(\mathrm{CH_3})_2$	C(C <sub>6</sub> H <sub>6</sub> )(C <sub>6</sub> H <sub>11</sub> )CN β-[Diethylaminoethyl]- (1-cyclolexenyl)phenyl-	ncetonitrile (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C(CN)C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>5</sub> )CN  Cl(Cl1 <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sup>2</sup> CN	(NCC(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> (C <sub>H</sub> <sub>2</sub> ) <sub>2</sub> CN Br(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN None	CH <sub>2</sub> CH <sub>2</sub> C(G <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> 	CH2CH2C(C6H5)2 		n-C <sub>3</sub> H <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN i-C <sub>3</sub> H <sub>7</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN	$CH_2 = CHCH_2C(C_6H_5)_2CN$ $CH_2 = CHCH_2C(C_6H_5)_2CN$ $CH_3CHCICH_2C(C_6H_5)_2CN$	$\text{Br}(\text{CH}_2)_3\text{C}(\text{C}_6\text{H}_5)_2\text{CN}$ $\text{CH}_2$ — $\text{C}(\text{C}_6\text{H}_5)_2$	п <sub>3</sub> ссн с=ин	$\begin{array}{ccc} \operatorname{CH}_{\mathbf{z}} & & & \operatorname{C}_{\mathbf{z}} \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & $	0
$(n \cdot \mathrm{C}_4\mathrm{H}_9)_2\mathrm{N}(\mathrm{CH}_2)_3\mathrm{C}!$	$(C_2H_5)_2N(CH_2)_2CI$	I.s.	$C_2$ $C_2H_5I$	Dr(CH <sub>2</sub> ) <sub>2</sub> Br CH <sub>2</sub> —CH <sub>2</sub>	CH2—CH2	CH <sub>2</sub> —CH <sub>2</sub>	$c_3$	$n$ - $C_3$ $H_7$ $I$	$\mathtt{CH}_2 = \mathtt{CHCH}_2\mathtt{Cl}$ $\mathtt{CH}_2 = \mathtt{CHCH}_2\mathtt{Br}$ $\mathtt{CH}_3\mathtt{CHClCH}_2\mathtt{Br}$	$Br(CH_2)_3Br$ $H_3CCH$ $CH_2$	0	H <sub>3</sub> CCH—CH <sub>2</sub>	

 $C_6H_5$ 

1-Cyclohexenyl

 $C_6H_5$ 

Note: References 577-1080 are on pp. 322-331. † The methylating agent was not specified.

# TABLE XIV-Continued

1055 1055 191,10551055 1055 191, 1055 191 1055 191 1043 1055 1055 178 1054 1004 171 178 ence Cells Liquid NII3 CeHe  $C_6H_6$ CoH 6  $C_6H_6$  $C_6H_6$ Solvent Ether  $C_6\Pi_6$  $C_6H_8$ Ether Celf  $C_6 \Pi_6$  $C_6II_6$  $C_6H_6$ CoH NaNH2 NaNH2 NaNH2 NaNH2 NaNII. NaNH2 NaN II2 NaNu2 NaNII NuNI NaNII2 NANH NANH NaNII. NANII: NaNII2 ALKYLATION OF MONONITRILES, RCH(R')CN ١ ł 06 ١ 83 85 ١ ١ ١ Cyclohexyl-[4-morpholinyl)- $\alpha$ -Pilenyl- $\alpha$ -(7-chloro-4-quinolyl)a-Plienyl-a-(5-chloro-4-quinolyl)-Cyclopentyl(cyclolicxyl)phenyl.  $\gamma$ -(electhylamino)butyronitrile 3-(alethylamioo)butyronitrile C(C6H5)(C6H11)CN (1-pyrrolidyl)butyronitrile (I-plperidyl)butyronitrile  $\alpha$ -Cyclohexyl- $\alpha$ -phenyl- $\gamma$ - $(c_2\Pi_4)_2\mathrm{NGH}(c_2\Pi_5)\mathrm{CH}_2\mathrm{Cl}\ (c_2\Pi_5)_2\mathrm{NGH}(c_2\Pi_5)\mathrm{CH}_2.$  $C_611_5C(C_211_5)(C_611_{11})CN$   $n\cdot C_211_7C(C_61I_5)(C_61I_{11})CN$ a-Cyclohexyl-a-phenyl-yусп'спо)-C(C,H,)(C,H,1)CN  $C_6 \Pi_5 C(C\Pi_3)(C_6 \Pi_{11})CN$  $(C_2H_5)_2NCH(C_2H_5)$ - $C(C_6H_5)(C_6H_{11})CN$ (CH<sub>3</sub>)<sub>2</sub>NCH<sub>2</sub>CH(CH<sub>3</sub>)-(CH<sub>2</sub>)2NC|1(CH<sub>2</sub>)CH<sub>2</sub>-C(C,II,)(C,II,1)CN C(C6H3)(C6H111)CN C(C,113)(C,1111)CN C(C,H3)(C,H11)CN Product (C,11,5)2N(CH2)2" (СП<sub>2</sub>)2N(СП<sub>2</sub>)2acctonitrile chloride hydrochloride chloride hydrochloride NCH2CH(CH3)CI (CII3)2NCII(CII3)CII2H (CII3)2NCH3CII(CII3)Br  $(C_2\Pi_5)_2N(C\Pi_2)_2Cl^{-1}lCl$ (CII3), X(CII4), CI-HCI  $(C_2\Pi_5)_2\mathrm{NCH}(C_2\Pi_5)\mathrm{Cl}$ h-(1-Pyrrolidyl)ethyl 4,5-Dichloroquinoline 4,7.Dictioroquinoline Cyclopentyl bromide h-(1-Piperidyl)cfliyl Alkylating Agent  $C_2 \Pi_3 \Pi_T$ CII3Xt C,113 (Cont.) 1 (CIII)N(CIII)

(1111) Cyclohexyl

CoHe

NaNII2

١

hutyllphenylacetonitrile

6-(4-MorpholinyI)butyI (C2H6)2NCH2C(CH3)2-

(C,H,),NCH,C(CH,)2. CH,C(C,H,)(C,H,1)CN

		_											
1055	1056	264	1004 1057	1057, 91 25	25	25	76	27	23, 523 27 25	1057 27		329	
$\mathbf{C_6H_6}$	Toluene	Ethanol	°н°э °н°э	C <sub>6</sub> H <sub>6</sub> Ethanol	$C_{6}H_{6}$	$\mathtt{C_6H_6}$	HO H. O. Lonoly V.	Xylene Xylene	$C_6H_6$ Xylene- $t$ - $C_4H_9OH$ $C_8H_6$	$c_4^{\mathbf{r}_6}$ $c_4^{\mathbf{r}_6}$		$C_6H_6$	
NaNH <sub>2</sub>	$NaNH_2$	$ m NaOC_2H_5$	NaNH <sub>2</sub> NaNH <sub>2</sub>	NaNH <sub>2</sub> NaOC <sub>2</sub> H <sub>5</sub>	$NaOC_2H_5$	$_{ m NaNH}_{ m 2}$	r n Jua	KOC4H9-1	KOC <sub>4</sub> H <sub>9</sub> -t NaNH,	NaNH2 KOC4H9-t		$NnNH_2$	
ł	31	100	88 70	74-80	52	57	0	8 22 3	42 47	57		80	
$(n \cdot C_4 H_{\mathfrak{g}})_2 N (CH_2)_3$ -	$C(C_6H_5)(C_6H_{11})CN$ $\beta$ -[Diethylaminoethyl]- (1-cyclohexenyl)phenyl-	avetonitrile (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C(CN)C(C <sub>6</sub> H <sub>6</sub> ) <sub>2</sub> CN	(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C(C <sub>2</sub> H <sub>5</sub> )CN (CI(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN	\\\ \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	('11,2CH,2C(C,H5)2 	cu <sub>2</sub> cu <sub>2</sub> cu <sub>3</sub> ) <sub>2</sub>	NO ( H O/O H O :	1.C.11,C(C(115)2CN :.C.11,C(C(115)2CN	$CH_2 = CHCH_2 C(C_6H_5)_2 CN$ $CH_2 = CHCH_2 C(C_6H_5)_2 CN$ $CH_2 CH CHCH_3 C(C_6H_2)_2 CN$	Br(CH <sub>2</sub> ) <sub>3</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN CH <sub>2</sub> ——C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub>	H <sub>3</sub> CCH C=NH	$CH_2$ $C(C_6H_5)_2$	$H_3$ ccu $\dot{c} = NH$
(#-C.H.),N(CH.),Cl	(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> Cl	I2	C <sub>1</sub> H <sub>5</sub> I	CICHI), Br CH2——CH2	CH <sub>2</sub> —CH <sub>2</sub>	cu <sub>2</sub> —cu <sub>2</sub>	C <sub>3</sub>	1-C3H,1	CH2=CHCH2CI CH2=CHCH2Br CH2CHCH4Br	Br(CH <sub>2</sub> ) <sub>3</sub> Br H <sub>3</sub> CCH	°	H <sub>3</sub> CCH——CH <sub>2</sub>	ò

C, 115

1-Cyclohexenyl

C<sub>6</sub>IIIs

 $C_{\mathbf{L}}H_{\mathbf{5}}$ 

Note: References 577-1080 are on pp. 322-331. f The methylating agent was not specified.

	RCH(R')CN
Jontinued	BCI
Ĭ	
TABLE XIV	

Refer-	55 55	25	1057,26	1025 1058 1057	27		27, 26, 91		25	i	1059			
	Solvent C <sub>6</sub> H <sub>6</sub>	$\mathtt{C}_{\mathfrak{q}}\mathtt{H}_{\mathfrak{q}}$	CAH	Toluene Ethanol C <sub>6</sub> H <sub>6</sub>	Xylene-LC4H9OII		# 5	<b>C</b> 6118	1	$C_6H_6$	<b>\$</b>	C <sub>6</sub> H <sub>6</sub>		
H(R)CN	Yield, % 69 NaNH2	71 NANH2		70 NaNH2 92 NaNH2 90 NaOC <sub>2</sub> H <sub>5</sub> 30 NaNH <sub>2</sub>	T SOM	ca. 46 NUC41197	ca. 46	ea. 39 NaNH2	ca. 39	36 NaNH2	l	Low NaNH2	0	
ATTACK OF MONONITRILES, RCH(R')CN	Product CII2 —— C(C <sub>6</sub> H <sub>5</sub> )2	H <sub>3</sub> CrH CO	CH <sub>2</sub> =ChrCH <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C.	(CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>3</sub> ) <sub>2</sub> CN (CH <sub>3</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>3</sub> ) <sub>2</sub> CN C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> CCH <sub>2</sub> C(C <sub>6</sub> H <sub>3</sub> ) <sub>2</sub> CN T <sub>2</sub> CO <sub>2</sub> C(C <sub>2</sub> H <sub>2</sub> C <sub>2</sub> N	**************************************	(CH <sub>2</sub> ) <sub>2</sub> NCH(CH <sub>3</sub> )CH <sub>2</sub> -	$\begin{pmatrix} C(C_6H_5)_2^{CN} \\ (CH_3)_2^{NCH}_2^{CH}(CH_3)^2 \end{pmatrix}$	C(C6H5)2CN (CII3)2NCH(CH3)CII2	C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN (CH <sub>2</sub> ) <sub>2</sub> NCH <sub>2</sub> CH(CH <sub>3</sub> )-	C(C,H,)2CN (CH,)2NCH(CH,)CH2-	C(C,H3)2CN (CH3)2NCH2CH(CH3)-	( C(C,H <sub>5</sub> ) <sub>2</sub> CN (NC(CH <sub>3</sub> ) <sub>2</sub> CH(CH <sub>3</sub> )-	C(C,H,),CN	(CoH.s)2
NOTTA TUCK	Alkylating Agent	H <sub>3</sub> CCA H <sub>3</sub>	CH2=CBrCH3Br CI	2),2G 2),2G 2,1,5		C <sub>s</sub>	(CII.),NCH2CII(CH3)Cl		CH ).NCH,CH(CH <sub>3</sub> )Cl		CH.),NCH(CH.)CH2CI		NO CHANGE TO	CH <sub>3</sub> CHCNCLL <sub>2</sub> /2CT

н С<sub>е</sub>П<sub>S</sub>

	CICH2CH(CH3)CH2CN	NCCH2CH(CH3)CH2-	1	NaNH;	$c_{s}$ H $_{s}$	1059
	$\mathrm{Br}(\mathrm{CH}_2)_2\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5$	C(C,H3)2CN C2H3O2C(CH2)2C(C,H3)2CN	ea. 75	ca. 75 NaNII2	Calls	1053
	ນ					
	(C <sub>2</sub> H <sub>5</sub> O) <sub>2</sub> CHCH <sub>2</sub> Cl	(C <sub>2</sub> II <sub>5</sub> O) <sub>2</sub> CHCII <sub>2</sub> C(C <sub>6</sub> II <sub>5</sub> ) <sub>2</sub> CN	1 8	NaNII,	Çın	1000
	(C <sub>2</sub> (1 <sub>5</sub> ) <sub>2</sub> N(C(1 <sub>2</sub> ) <sub>2</sub> Cl	(C2115)2-3 (C112)2-C (C4115)2-CN	20.0		ָרֶבֶּּ בַּרְבִּי	1057
	p-(1-ryrrollayl)ctnyi chloride hydroehloride	a,a-14pnenyi-y-(1-pyrrollayi)- butyronitrile	ž	Nan II.	C <sub>6</sub> 11 <sub>6</sub>	1057, 191
	β-(4-Morpholiny1)ethyl	a.a.Dlphenyl-y-(4-morphollnyl)-	26	NaNH <sub>2</sub>	CeIIs	1057
	chioride $\beta$ -(1-Piperldyl)ethyl chloride	bucyronicne \$\alpha \text{Diphenyl-y-(1-piperidyl)-} butyronitrile	73	NaNH,	CeIIs	91, 93, 1057
	ບ້					
	(C,II,),N(CII,),C)	(C,II,),X(CII,),C(C,II,),CN	1	NaXII.	11 0	*
	$(C_2\Pi_3)_2$ NC $\Pi_2$ C $\Pi$ (C $\Pi_3$ )Cl		1	NaNH2	Calle	1001
		(C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub> NCH(CH <sub>3</sub> )CH <sub>2</sub> - C(C <sub>4</sub> H <sub>3</sub> ) <sub>2</sub> CN				
	Cellsch 2CI	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> ),CN	83	NaOC.11.	Felianoi	9
	CoH,CH2CI	Censchool Constant	1	NaN II,	Ether	700
	Cellscii ci	C,H, CH,C(C,H,S),CN	66	KNII,	Liquid NII, ether	195
	p-(z-metnyt-1- pyrrolidyl)ethyl chloride	α,α-Diphenyl-γ-(2-methyl- I-pyrrolldyl)butyronltrile		NaNII <sub>2</sub>	روالو	161
	fyllethyl	$\sim \sim Diohomul_{-1}$ (1 where then				
		butyronitalle	1	NaNH <sub>2</sub>	СеНв	56
	1-(4-Morpholinyl).	$\int_{\alpha,\alpha-D}  phenyl-y-(4\cdot morphollnyi)-$ valeronitrile	<u>s</u>	NaNII.	$C_{\mathbf{g}}H_{\mathbf{g}}$	25, 91
	Z-caloropropane	\(\alpha, x-Dlphenyl-y-(4-morphollnyl)-\) i-valeronitrile	32			
••	hollnyl)propyl	$(\alpha, \alpha \cdot \text{Diphenyl-}\gamma \cdot (4 \cdot \text{morphollnyl}) \cdot \text{valeronitile}$	30	NaNII;	Сене	25
	chloride	a,a.Diphenyl-7-(4-morpholinyl)-	50			
) are on pp. 322-331	322-331	1-valeronitrile				

Nak: References 577.–1030 are on pp. 322–331.

## TABLE XIV-Continued

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	ORG.	ANIC R	EACTION	NS		
	Refer- ence	195 1061	91, 1061, 1062	1063	1057 1093	1063
	Solvent	Liquid NH3-ether G <sub>6</sub> H <sub>6</sub>	$C_6H_6$	$c_{ m kH_8}$	С <sub>6</sub> .Н. <sub>6</sub> С <sub>6</sub> .Н. <sub>6</sub>	C <sub>6</sub> H <sub>6</sub>
C)CN	, Base	$KNH_2$ $NaNH_2$	$NaNH_2$	NaNH2	NaNH <sub>2</sub> NaNH <sub>2</sub>	$NaNH_2$
H(B	Yield, %	89	1	11	81 81	16
ALKYLATION OF MONONITRILES, RCH(R')CN	Product	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN a,a-Diphenyi-6-(1-piperidyl)-	vactonume α,α-Diphenyl-γ-(1-piperidyl)- valeroultrile and α,α-Diphenyl-γ-(1-piperidyl)- i-valeronitrile	$\mathrm{C_6H_5N}(\mathrm{CH_2})(\mathrm{CH_2})_2\mathrm{C}(\mathrm{C_6H_5})_2\mathrm{CN}$	(nC,H <sub>0</sub> ) <sub>2</sub> N(CH <sub>2</sub> ) <sub>2</sub> C(C <sub>6</sub> H <sub>2</sub> ) <sub>2</sub> CN C <sub>6</sub> H <sub>2</sub> CH <sub>2</sub> N(CH <sub>3</sub> )(CH <sub>2</sub> ) <sub>2</sub> . C(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> CN	Cehschin(ch3)chz- Ch(ch3)c(Gh4)2CN Cehschin(ch3)c Ch1;ch2n(ch3)- Ch2;ch23cn
ALKYLAT	Alkyiating Agent	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )Ci y-(1-Piperldyl)propyi	chloride 1-(1'-Piperidyi)- 2-chloropropane	$C_{\mathfrak{g}}$ $C_{\mathfrak{g}}H_{\mathfrak{g}}N(\mathrm{CH}_{\mathfrak{g}})(\mathrm{CH}_{\mathfrak{g}})_{\mathfrak{g}}\mathrm{C}\mathfrak{f}$	$G_{10}$ $(n \cdot C_{\epsilon}H_{\epsilon})_{\epsilon}^{N}(\mathrm{CH}_{\epsilon})_{\epsilon}^{C}\mathrm{Ci}$ $C_{\epsilon}H_{\epsilon}^{\epsilon}\mathrm{CH}_{\epsilon}^{\epsilon}N(\mathrm{CH}_{\epsilon})_{\epsilon}^{C}\mathrm{Ci}$ $C_{\epsilon}H_{\epsilon}^{\dagger}$	C <sub>11</sub> C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N(CH <sub>3</sub> )- CH <sub>2</sub> CH(CH <sub>3</sub> )Cl
		(Cont.)				

### TABLE XV

:				·	IKGAN.	IC K	BAUI	TONO				
Rofer- enco	193	193	193	193	193	171	171	259 192			Reforence 1065	1066 340 346 1065
Coleont	C <sub>6</sub> H <sub>6</sub>	$C_6H_8$	$C_6H_6$	C,H,	C,H	$C_{\mathfrak{g}}H_{\mathfrak{g}}$	Ethor	Ethanol				
	Base NaNH2	$NaNH_2$	$NaNH_2$	NaNH.	NaNH	$NaNH_2$	$NaNH_2$	NaOC <sub>2</sub> H <sub>5</sub>	17 at 17 17 2	7	1 leid, %	90   80
Yield,	%	١	65	١	1	83	7.2	3	50 50	Acids		
ALKYLATION OF ALKYLIDENEACETONITULES	Alkylating Agent		ıyı		$\beta$ -(1-Piperidyl)ethyl $\alpha$ -(1-Cycloponteny-) $\alpha$ -(1-piperidyl)butyronitrile elloride $\alpha$ -(1-Cyclopontenyl)- $\alpha$ -( $p$ -methoxy-(CH <sub>2</sub> ) <sub>2</sub> Cl $\alpha$ -(1-Cyclopontenyl)- $\alpha$ -( $p$ -methoxy-( $p$ -methoxy- $q$ - $q$	phenyl)-y-{unitenty minney} butyronitrile		${ m ICH_2}$ ${ m Br}$	$\mu$ - $\nu_{\rm s}$ $\mu$ - $\nu_{\rm s}$ $\mu$ - $\nu_{\rm s}$ $\mu$ - $\nu_{\rm s}$ $\mu$ - $\nu$	TABLE XVI REDITCTIONS LEADING TO ALKYLMALONIC ESTERS OR ACIDS	Reducing Product	$H_2$ —Ni $CH_3CH(CO_2C_2H_5)_2$ $AlHg_x$ $C_2H_3CH(CO_2C_2H_5)_2$ $H_2$ —Pd/C $C_2H_3CH(CO_2C_2H_5)_2$ $H_2$ —PdCl; $C_2H_3CH(CO_2C_2H_5)_2$ $H_2$ —Ni $C_2H_3CH(CO_2C_2H_5)_2$
	Commented Alkylated	Cyclopentylidene-(2-thienyl)-	acetonitrie	Cyclopentylidene(phenyl).	nectonitrie	Cyclopentylidene (P-mexic.) phenyl)acetonitrile	Cyclohexylidene(phonyl).				Dodwood	CH <sub>2</sub> =C(CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> $CH_2CH=C(CO_2C_2H_5)_2$

			c	0,0
C.II.CII C(CO.C.II.),	H,—Pd/C	n.C,H,CH(CO,C,H,sl,	96	340
(CII.).C= C(CO.C.II.).	H,—Ni	i.C,H,CH(CO,C,Hs),	96	340, 1068
n.('.11.('.11('.('.0,'.2.11.)'.	H,—Pd/C	11.C,H,CH(CO,C,H,1),	93 - 96	340
M	II,—Ni	n-C,H,CH(CO,C,H,S),	95	1065
C,II,C(CII,)=C(CO,C,II,),	II,*	C, H, CH(CH, )CH(CO, C, H, s),	95-100	1067
CH; ~ CH(CH,), CH=C(CO,C,H,),	II,—Pd/C	$n \cdot C_s H_{11} CH(CO_2 C_2 H_s)_2$	79	277
5.C,11,CH: - C(CO,C,H;),	H,—Pd/C	:-C,H,1CH(CO,C,H,),	60-96	340
Diethyl cyclopentylidenemulomate	H**	Diethyl cyclopentylmalonato	95-100	1067
Diethyl 2-cyclopentenylmalonato	II,—PtO.	Diethyl eyelopentylmalonato	66	927
Purfurylidenemnlonic acid	NaHg.	Furfurylmalonic acid	ļ	355
Diethyl furfurylidenemalonate	H,-Ni	Diethyl furfurylmalonato	96	1069, 1065
2.Thenylideneundonic neid	NaHg,	2.Thenylmalonie aeid	85	358
Diethyl (2-pyrrylmethyleno)midonate	$H_2-PtO_1$	Diethyl (2.pyrrolidyImethyl)malonate	95	1070
CH; CHCH;C(NHCOCH;)(CO;C;H;);	H,—Ni	$n \cdot C_3 H, C(NHCOCH_3)(CO_2C_2H_3)_2$	ļ	232
CHICHE CHCHE(NHCOCH!)(COICHI);	II <sub>2</sub> —Ni	$n \cdot C_4 H_s C(NHCOCH_3)(CO_2 C_2 H_5)_s$	ŀ	442
n-C <sub>4</sub> 11 <sub>13</sub> CH==C(CO <sub>4</sub> C <sub>4</sub> H <sub>5</sub> ) <sub>2</sub>	H,—Ni	$n\cdot \mathrm{C}_{t}\mathrm{H}_{13}\mathrm{CH}(\mathrm{CO}_{2}\mathrm{C}_{2}\mathrm{H}_{5})_{2}$	16	1065
C,II,C11=-C(CO,II),	NaHg,	C,H,CH,CH(CO,H);	ļ	354
C,II,CII. C(CO,C,II,),	AlHg,	C,H,CH,CH(CO,C,H,),	00	350, 343
	$H_2$ —Ni	C,H,CH,CH(CO,C,H,s),	97	1065
p-C11,0C,11,C11-C(C0,C,11,),	H,—Ni	p-CH <sub>3</sub> OC,H <sub>3</sub> CH <sub>2</sub> CH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	100	950, 360, 1071
Diethyl (2,5-dimethoxybenzylidene)- malonate	H2*	Diothyl (2,5-dimothoxybenzyl)malonate	ļ	1072
(2,3,4.Trimetlylbenzylidene)malonic acid	H,—Pd	(2,3,4-Trimethylbenzyl)malonie acid	ļ	361
Diethyl di (2 eyelopentenyl)malonate	H,—Ni	Dietliyl difevelopoutyl)malonato	I	100
Directhyl phenyl (2-cyclohexenyl)malona(o	H,—PtO,	Dimethyl phonyl(evelohoxyl)malonato	06	534
Dirthyl allyl-(\beta-naphtliyl)malonate	$H_1$ — $Pd/C$	Diethyl n-propyl-(B-naphthyl)malonato	83	959
Digitized allylic (9-phenonthryl)malonato	H;-Pd/C	Diethyl n-propyl-(9-phenanthryl)malonato	98	955
Note: References 577-1080 are on pp. 322-331.	2-331.			

بالمعاشدوة وتويير

\* The entalyst employed was not stated.

### TABLE XVII

TON OF THE ALEVLIDENE AND ARYLDBENE DERIVATIVES OF

Reforence	163	363	363	1073,363 $340$	363	277	340, 363 363	351	363 575	340	351 363	363 363	317	363 363		
Yiold,	SO-85	\$6 50	63 90-93	90-1-6	96 86	66 67	90–97	96 70	41-63	84 03	84 91–98	11.	= 1	39 73-81		
Reduction of The Alemantic Peters, And Alemantic Vernoachtic Acid, Cyanoachtic Acid,	Product	C, H, CH(CN)CO, C, H, 5	.C,11,CH(CN)CO,C,11,5 : C,11,CH(CN)CO,C,11,5	Collicial CH(CN)COlours	C. II, CH (CH, ) CH,	i.c.11,c11(CN)CO.c.11;	n.GH(GH3)CH(CN)2	".C.H.,CH(CN)CO;C;Hs	Ethyl cyclopentylcynnoncetato	Enyl (1,3-dimond) ;-C,H,CH(CH,3)CH(CN)CO,CH,3	Ethyl cyclohoxylcynnoncolulo Ethyl cyclohoxylcynnoncoluto	Ethyl cyclohexyleyanoacetato	Ethyl n-nepoles Ethyl (1-methylhoxyl)cyanoacetate			
OF THE AREA	Reducing	Media :	II,—rafe	Milg, II,—Pd/C	11,—Pd/C	H,-Pd/C	11,—Pd/c	II,—Palo	M. Trufc	H,—Pd/C	H,—Pd/c	MHg, H,—Pd/C	H;—Pd/C	H,—Pd/SrCO,	H,—Pa/c	
(YANOACHTIC		Compound Reduced	CHICHO + CHI(CN)COICHI	C115CHO+CH4(CN)CO2CH13 (CH3)C - C(CN)CO2CH13	('III),CO + CH,(CN)CO,C,H3	C,11,C(C(1,1)=C(CN)CO,C,11,	6.C.1(1,CH(0+CH,1CN)CO3C173 6.C.1(1,CH(0H)CH,1CN)CO3C113	n.C,11,C(C11,)=C(CN),	1.C.11,C110+C11,(CN)CO,C111	Ethyl cyclopentylidenceynolucy	(CII), C=CIC(CII) = C(CN)CO, CH,	Ethyl cyclohexylidenceyanoacetato	Cyclohexanono+Citi(Cx)CO <sub>2</sub> C <sub>2</sub> H <sub>2</sub>	$0.0_1 II_1 COCII_2 + CII_3 (CN) CO_2 C_2 II_3$	(n.C,11,),co + c11,(cN)CO,C,11, n.C,11,,coc11, + C11,(cN)CO,C,Hs	

353	352	352	357 993	363, 364 357	357	351	357	357	340	217	362	362	362	362	340	362	
1	83	87	ea. 85 86	63 ca. 85	ea. 85 ca. 85	72	ca. 85	ea. 85	<del>7</del> 6	51	30	38	35	t- 61	09	35	
Ethyl (2-methyleyclohoxyl)cyanonestate	Bthy! (3-methyleyelohexy!)eyanoacetate	Bihyl (4-mothyleyelohexyl)cyanoncetate	C,H,CH,CH(CN)CO,H C,H,CH,CH(CN)CO,C,H;	C,H,CH,CH(CN)CO,C,H,s o.HOC,H,CH,CH(CN)CO,H	m-HOC,H,CH,CH(CN)CO,H	Ethyl eyeloheptyleyanoacetate	p-Methoxybenzyleyanoacetie aeid	(3,4.Methylenedioxybenzyl)cyanoacetic acid	$C_aH_aCH_aCH(CH_a)CH(CN)CO_aC_aH_a$	Ethył 1-indanyleyanoacetato	$(C_2H_5O_2C)_2CH(CH_2)_3CH(CN)CO_2C_2H_5$	(C,H,O,C),C(C,H,)(CH,),CH(CN)CO,C,H,	(C <sub>2</sub> H <sub>5</sub> O <sub>2</sub> C) <sub>2</sub> C(OCOCH <sub>3</sub> )(CH <sub>2</sub> ) <sub>3</sub> - CH(CN)CO <sub>3</sub> C, H <sub>2</sub>	(C,H,O,C),C(XHCOCH,)(CH,),- CH(CN)CO,C,H,	o-C,H,C,H,CH,CH(CN)CO,C,H,	(C,H,O,C),C(C,0,H <sub>21</sub> -n)(CH <sub>2</sub> ),- CH(CN)CO,C,H,	
$ m AHIg_z$	$AIHg_x$	AIIIg,	NaHg <sub>z</sub> NaHg <sub>z</sub>	H <sub>1</sub> —Pd/C	NaHg,	AIHg.	NaHgz	NaHgr	II,—Pd/C	11,-Pd/C	11,—Pd/C	II;—Pd/C	H2-Pd/C	H,—Pd/C	H,—Pd/C	H <sub>1</sub> —Pd/C	
F4byl 2-methyleyelohexylidenceyano-	ncetato Ethyl 3-methyleyeloftexylidenecyano-	acetato Ettyl Emethyleyelohexylidenceyano-	nectate C_H_CH_CH ~ C(QN)CO_4H	CHECHO CONTOSTINA CHECHO FURCONCOLLIA	m-HOC,H,CH=-C(CN)CO,H	2,1.Dihydroxybenzyhdenegyanoneette ueta Edast eedabentyhduneevunoneetuto	" (II:00:11; clcx)(0*11	Physial dence y unoncetic acid	Callactif (CH) = C(CN)CO, Calla	Ethyl Lindanylidenecyanoncetate	(C,H,O,C),CH(CH,),CHO ;- CH,(CN)CO,C,H,	(C,H,O,C),C(C,H,)(CH,),CHO+ CH,(CN)CO,C,H,	(C,H,O,C),C(OCOCH,)(CH,),CHO+	(C,11,0,C),C(NHCOCH,)(CH,),CHO+ CH,(CN)CO,C,H,	"C,11,C,11,C1F-C(CN)CO,C,11,	('','',','','','','','','','','',''',''	

Note: References 577-1080 are on pp. 322-331.

### TABLE XVIII

	Yiold,
Esters	
ONO I COMMISSION OF THE PERSON	Abbition of Chignand Reagents to Alkylipharamond of Chigh,
	10
	REVOUNTS
	GHONNID
	.10
	Nonting,

% Reference	37 157	01	40 367	9 1	82 954, 156 1074	ខា	C.H.), — 829	7.	C,H,), - 1074	00	(s) <sub>2</sub> 32 829	
Profligt	(CII,),CCII(CO,C,II,),	n-C,II,C(CII,),CII(CO,C,II,);	(CH <sub>2</sub> ) <sub>2</sub> CHCH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> ) <sub>2</sub>	C, II, C(CII,), CH(CO, C; 15,15,15,15,15,15,15,15,15,15,15,15,15,1	(c <sub>4</sub> H <sub>3</sub> );CHCH(CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub> );	OCHIC HICH(CLHS)CHICO C	p.CH.C.H.CH(Certs)CH(CO;C.H.s);			CHCHCHCOOCH ()	(p.CH,OC,H,),CHCH(CO,C,H,S),	•
Appeties of the second	Grignard Bengent	CH3NRI n-C <sub>1</sub> H4NRHr	n.C,H,MgBr	C.H.MRBr C.H.CH.MgCl	CH <sub>3</sub> NgI	O.C.II.C.III.MRB	p.CH,CeH,MgBr	p.CII,OC,II,MgBr	z.Naphthylmagnesium bromide	C. H.MgBr		p.CH3OCartingto
	Alky lideno Later	(CH))(C+ C(CO <sub>2</sub> C;H))			C,11,C11 C(CO,C,115)2					CH OCHECH COCO, C. 113);	p.(11,C,11,C11= C(CO,C,Hs);	".(11,0C,11,CII=C(CO,C,111s),

### TABLE NIX

### % ADDITION OF CHIGNARD REAGENTS TO ALKYLIDENECYANOAOETIC ACIDS AND ESTERS AND TO ALKYLIDENEMALONONITRILES Product C,H,CH,C(CH,),CH,CN "-C,H,C(CH,),CH,CN C,H,C(CH,),CH,CN Grignard Reagent ".C,II,MgBr C,H MgBr Alkylidene Derivative

Reference

367 367 367 367 367

n-C,H,C(CH,),CH,CN

C,H,CH,MgCl n.C,H,MgBr C,H,MgBr

(CH3)3C+C(CN)CO3K

(CII,), C-C(CN)CO,II

C.H.C(CH.),CH,CN

41 60 68 17 30

11-C, II-3MgBr   C, II-4   C, II-3MgBr   C, II-4   C, II-3MgBr   C, II-4   11-C, II-4   II-4	m-c, m, c(c, m), c, m, c,	15 63 85 49 41 41 31 - 44 39 85 33 34 34 34 34 34 34 34 34 34 34 34 34	367, 159 367 159 159 368, 1075 368, 1075 368, 1075
Colling of	H, CH, C(CH, CH(CN) CO, C, H, H, CH, C(CH, CH(CN) CO, C, H, H, C(CH, L, CH(CN) CO, C, H, H, C(CH, L, CH(CN) CO, C, H, H, CH, C(C, H, CH, CH, CH, CH, CH, CH, CH, CH, CH	85 41 41 41 31 41 39 20 12 73 10-32 34 34	367 159 159 368, 1075 1075 368, 1075
Controlled Branch Branc	H,CH,C(CH,),CH(CN)CO,C,H, H,C(CH,),CH(CN)CO,C,H, H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, C,H,C(C,H,)(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH(CH,)CH(CN)CO,C,H, J,H,CH,HCH,CH,CH,CN,CO,C,H, J,H,CH,HCH,CH,CH,CN,CO,C,H, J,H,CH,HCH,CH,CH,CN,CO,C,H, J,H,CH,HCH,CH,CH,CN,CO,C,H,	41 41 41 31 41 39 20 12 73 10-32 34 54	159 159 368, 1075 1075 368, 1075 368, 1075
CH3MgI  n.C,H4MgBr  i.C,H4MgBr  i.C,H4MgBr  cc,H4MgBr  cc,H4MgBr  l.C,H4MgBr  l.C,H4MgBr	H,C(CH,),CH(CN)CO,C,H, -C,H,C(C,H,)(CH,)CH(CN)CO,C,H, -H,CH(CH,)CH(CN)CO,C,H, -C,H,C(C,H,)(CH,)CH(CN)CO,C,H, -L,H,CH(CH,)CH(CN)CO,C,H, -L,H,CH(CH,)CH(CN)CO,C,H, -L,H,CH(CH,)CH(CN)CO,C,H, -L,H,CH(CH,)CH(CN)CO,C,H, -L,H,CH(CH,)CH(CN)CO,C,H, -L,H,CH(CH,)CH(CN)CO,C,H, -L,H,CH(CH,)CH(CN)CO,C,H, -L,H,CH(CH,CH,CN)CO,C,H, -L,H,CH(CH,CH,CN)CO,C,H, -L,H,CH(CH,CH,CN)CO,C,H, -L,H,CH(CH,CH,CH,CN)CO,C,H, -L,H,CH(CH,CH,CN)CO,C,H, -L,H,CH(CH,CH,CN)CO,C,H, -L,H,CH(CH,CN)CO,C,H, -L,H,CH(CH,CH,CN)CO,C,H, -L,H,CH(CH,CN)CO,C,H, -L,H,CH(CH,CN)C	41 27-44 31-44 39 20 12 73 10-32 34	159 368, 1075 1075 368, 1075 368, 1075
n.C,H,NgBr i.C,H,NgBr i.C,H,NgBr sec.C,H,NgBr L,C,H,NgBr n.C,H,NgBr	-G,H;C(C,H;)(CH;)CH(CN)CO,C;H; ;,H;CH(CH;)CH(CN)CO,C;H; -C,H;C(C,H;)(CH;)CH(CN)CO,C;H; ;,H;CH(CH;)CH(CN)CO,C;H; ;,H;CH(CH;)CH(CN)CO,C;H; ;,H;CH(CH;)CH(CN)CO,C;H; ;,H;CH(CH;)CH(CN)CO,C;H; ;,H;CH(CH;)CH(CN)CO,C;H; ;,H;CH(CH;)CH(CN)CO,C;H; ;,H;CH(CH;)CH(CN)CO,C;H; ;,H;CH(CH;CH;CN)CO,C;H;	27-44 31-44 39 20 12-73 10-32 34	368, 1075 1075 368, 1075 368, 1075
	', H', CH(CH,)CH(CN)CO, C, H', -C, H, C(C, H,)CH(CN)CO, C, H', -L, H, CH(CH,)CH(CN)CO, C, H', -L, H, CH, CH, CH(CN)CO, C, H', -L, H, CH, CH, CH, CH(CN)CO, C, H', -L, H, CH, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CH, CN, CO, C, H', -L, H, CH, CH, CH, CH, CH, CH, CH, CH, CH,	31-44 39 20 42 73 10-33 34 54	368, 1075 368, 1075 368, 1075
	C4H;C(C,H;)(CH;)CH(CN)CO;C;H; ;,H;CH(CH;)CH(CN)CO;C;H; ;;H;CH(CH;)CH(CN)CO;C;H; ;;H;CH(CH;)CH(CN)CO;C;H; ;;H;CH(CH;)CH(CN)CO;C;H; ;;H;CH(CH;)CH(CN)CO;C;H; ;;H;CH(CH;)CH(CN)CO;C;H; ;;H;CH(CH;)CH(CN)CO;C;H; ;;H;CH(CH;)CH(CN)CO;C;H; ;;H;CH(CH;CH;CN)CO;C;H;	39 10 73 10 31 31	1075 368, 1075 368, 1075
	',',',',',',',',',',',',',',',',',',',	20 12 73 10-33 34 55	368, 1075 368, 1075
is is	-c,11,C(C,11,)(Cft,)CH(CN)CO,C,11, ;,H,CH(Cft,)CH(CN)CO,C,11, -C,H,C(C,H,)(CH,)CH(CN)CO,C,11, ;,H,CH(CH,)CH(CN)CO,C,11, ;,H,CH(CH,)CH(CN)CO,C,11, THOMORY CHANGES	10-32	368, 1075 368, 1075
	';H;CH(CH;)CH(CN)CO;C;H; -C;H;CH(CH;)CH(CN)CO;C;H; -;H;CH(CH;)CH(CN)CO;C;H; -cc-C;H;C(C;H;)(CH;)CH(CN)CO;C;H;	34 33	368, 1075
in the state of	-C,H,C(C,H,)(CH,)CH(CN)CO,C,H, 2,H,CH(CH,)CH(CN)CO,C,H, rec-C,H,C(C,H,)(CH,)CH(CN)CO,C,H,	# # °	368, 1075
in in	2,H,CH(CH,)CH(CN)CO,C,H, cc-C,H,C(C,H,)CH(CN)CO,C,H,	# 0	
	rec-C <sub>1</sub> H,C(C <sub>2</sub> H <sub>3</sub> )(CH <sub>1</sub> )CH(CN)CO <sub>2</sub> C <sub>2</sub> H <sub>3</sub>	9	
	II OTTONI SCHOOL STATE	c	107.5
,	しょこうしょ (しこり)しょ (しこく)しょしょしょ	01	
, , , , , , , , , , , , , , , , , , ,	1.C,11,C(C,11,)(CH,)CH(CN)CO,C,11,	es	107.5
	CII,CH(CII,)CH(CN)CO,CH,	63	
_	"-C,H,C(C,H,)(CH,)CH(CN)CO,C,H,	S.	1075
	C.H.CH(CH.)CH(CN)CO.C.H.	ei ei	
	"-C4H12C(C3H5)(CH1)CH(CN)CO2C3H5	Ç	1075
_	C,H,CH(CH,)CH(CN)CO,C,H,	÷.	
3	,H,C(C,H,)(CH,)CH(CN)CO,C,H,	79	367
•	"CIC, II, C(C, II, )(CII, )CII(CN)CO, C, II,	73	367
	S,H,CH,C(C,H,)(CH,)CH(CN)CO,C,H,	88	367
n-C <sub>4</sub> H <sub>9</sub> MgBr ( $n$ -(	n.C,H,C(CH,),CH(CN),	35	367
_	(CH <sub>3</sub> ), CHCH(CN);	19	
	C,H,C(CH,),CH(CN),	9	367
C,H,CH,MgCl C,I	C,H,CH,C(CII,),CH(CN),	92	367

Note: References 577-1080 are on pp. 322-331.

	1076	1077	1076	994 994	994 994	994	!	1077				Reference 278, 180, 1078	278
	.5 <del>.</del>	44	<b>‡</b>	1 1	1 1	1		14				Solvent C <sub>a</sub> H <sub>6</sub>	None
тю Легоя				1 2 2 1 2 2 1 2 2 2 2 2 2 2 2 2 2 2 2 2	23	CH.					tic Acids	Catalyst H <sub>2</sub> SO <sub>4</sub>	HCI
YEOYANOACE	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	CO2C2IIs	)CO,C,H,	H(CN)CO <sub>2</sub> C <sub>4</sub> F	N)CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		CH(CN)CO,C,H,			4D TARTROY Vield	33	1
TABLE XIX—Continued  TABLE AIX—Continued  ACIDS  AC	AND ESTERS AND TO ALKYLIDENEMALONOMIANA AND AND AND TO ALKYLIDENEMALONOMIANA AND	CH(CN)CO,C,IIs	C4115 CH(CN)CO4C4H5	CoH, CII(CH,)CH(CN)CO,CH,	Call CH(Ch, 1) Ch(Ch)Co, 2; 13 (Call s), CHCH(CN)CO, CaH;	Ċ <sub>6</sub> H;C≒CCH(C <sub>6</sub> H;)CH(CN)CO;C <sub>2</sub> H; α.C <sub>10</sub> H;CH(G <sub>6</sub> H;)CH(CN)CO;C <sub>2</sub> H;	C,Hs	CHICN	co.c.H.	xx	ARYLATION OF DERIVATIVES OF MESOXALIC AND TARTRONIC ACIDS	luct s)2	$O_{\mathbf{z}}C_{\mathbf{z}}\mathbf{H}_{\mathbf{z}})_{\mathbf{z}}$
TABLE XIX—Continued REAGENTS TO ALKYLIDE	id to Alky	,	$\sim$	/ J	<b>3</b> 5			<i>&gt;</i>		TABLE XX	TIVES OF M	Product (C,Hs),C(CO,C2Hs);	(p.HOC,H4)1C(CO1C1H1)1
TA T GRASSIED F	Estens AN	[g]3r	"C. H., Mußr	, ja	i.Ciff,MgBr	Callsakin CallsC=CMgBr a.Naphthylmagnesium		lgBr		22–33I.	OF DERIVA		(p.F
30	Delition of AND Coll.MgI	C. II, MRBr	1.5.4	JaK.16.	ויטין ויטיון	Callynging CallyC=CN ANaphthy		C,II,MgBr		are on pp. 3	ARYLATION	Arylating Agent C.H.	с,нон
•				:	50,50,713			,C,II,		сея 577–1080			ร์ บั
	,	gyanoacetate cyanoacetate			Callacter C(CN)CO3C4415			C(CN)CO,C,III,	; ;	CO <sub>1</sub> C <sub>1</sub> U <sub>3</sub> Note References 577-1080 are on pp. 322-331.		Compound Arylnted	00(0040411311
		Ξ ີ			ີ້			$\bigvee$	١			ئ ق	5

	CH,C,H,	(p.CH,C,H,),C(CO,C,H,),	1	H.SO.	Toluene	8701 878 9701	
	CH3OC, Hs	$(p\text{-CH}_3\text{OC}_4\text{H}_4)_{\scriptscriptstyle 2}\text{C}(\text{CO}_3\text{C}_2\text{H}_6)_{\scriptscriptstyle 2}$	1	H <sub>2</sub> SO <sub>4</sub>		1080	
	CH <sub>3</sub> OC,H <sub>5</sub>	$(p\cdot \mathrm{CH_3OC_4H_4})_2\mathrm{C}(\mathrm{CO_2C_2H_6})_2$	1	SnC1,	Anisolo	371	
OC(CO2CH3)2	CH <sub>3</sub> OC <sub>6</sub> H <sub>5</sub>	(p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> ) <sub>2</sub> C(CO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	i	$H_2SO_4$	Anisele	1080	
OC(CO2C2H5)2	о-сызсынон	Diethyl di-(4-hydroxy-	99	HCI	None	278	
	p-CH,C,H,CH,	o-meony phieny functionare Diethyl (2.5-dimethylphenyl).	51-57	5	a Virlano	c t	
		tartrenate	5	To ma	p-txyigiio	016	
	o-CH3C,H4CH3	Diethyl di-(3,4-dimethylphenyl)-	1	$H_2SO_4$	c-Xylone	1079	
OC(CO2CH3)2	o-CH3C,H4CH3	malonate Dimethyl di-(3,4-dimethylphenyl).	1	$H_2SO_4$	o-Xylene	1079	
	C2H5OC4H5	malonate Dimethyl di- $(p$ -ethoxyphenyl).	I	H,SO,	Phenetole	1080	
$\mathrm{OC}(\mathrm{CO}_{\mathfrak{s}}\mathrm{C}_{\mathfrak{s}}\mathrm{H}_{\mathfrak{b}})_{\mathfrak{s}}$	$\mathrm{C_2H_{5}OC_6H_{5}}$	malenate Diethyl di- $(p ext{-ethoxyphenyl})$ .	ı	H <sub>2</sub> SO,	Phenotole	1080	
	$lpha \cdot \mathrm{Naphthylmagnesium}$ bramidə	malonate $^{lpha ext{-}} ext{C}_{ar{1}ar{6}} ext{H}_{ar{5}} ext{C}( ext{COCOC}_{ar{6}} ext{H}_{ar{5}})_{ar{2}}$	1	1	Ether-teluene	372	· Or
	9-Phenanthryl- magnesium bramide	$9.\mathrm{C_{14}H_{5}C(OH)(CO_{2}C_{2}H_{5})_{2}}$	46	1	Ether-toluene	372	1001.
C <sub>6</sub> H <sub>5</sub> C(OH)(CO <sub>2</sub> C <sub>2</sub> H <sub>6</sub> ) <sub>2</sub> <i>p</i> ·CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> . C(OH)(CO <sub>2</sub> C <sub>5</sub> H <sub>6</sub> ),	CH <sub>3</sub> C <sub>4</sub> H <sub>3</sub> C <sub>4</sub> H <sub>6</sub>	$\begin{array}{ll} P\text{-}\mathrm{CH_3C_6H_4C(C_6H_5)(CO_2C_2H_5)_2} \\ P\text{-}\mathrm{CH_3C_6H_4C(C_6H_3)(CO_2C_2H_5)_2} \end{array}$	1 1	H <sub>2</sub> SO <sub>4</sub> H <sub>2</sub> SO <sub>4</sub>	Toluene C <sub>e</sub> H	1079	ELLIN IL
$p ext{-}(\mathrm{CH}_3)_2\mathrm{NC}_6\mathrm{H}_4^{-}$ $\mathrm{C}(\mathrm{OH})(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	$\mathrm{C_{6}H_{5}N(CH_{3})_{2}}$	$[p\cdot(\mathrm{CH_3})_2\mathrm{NC}_4\mathrm{H_4}]_2\mathrm{C}(\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5)_2$	80	POC13	$C_6H_5N(CH_3)_2$	373	111111
	$\mathrm{C_6H_6N}(\mathrm{C_2H_5})_2$	$p \cdot (C_2 H_5)_2 N C_6 H_4$ -	1	Poc1,	C.H.N.C.H.		AT T T
$p ext{-}(\mathrm{CH_3})_2\mathrm{NC_6H_4} ext{-}$ $\mathrm{C}(\mathrm{OH})(\mathrm{CO_9CH_3})_2$	$\mathrm{C_6H_5N(CH_3)_2}$	$C[C_6H_4N(CH_3)_2\cdot p](CO_2C_2H_6)_2$ $[p\cdot(CH_3)_2NC_6H_4]_2C(CO_2CH_3)_2$	1	Poď,	C.H.N(CH.).		ابتعدده
	$\mathrm{C_6H_5N}(\mathrm{C_2H_5})_2$	$p\cdot (\mathrm{C_gH_5})_2\mathrm{NC_gH_4}$ .	1	, DOG			,
p.(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> - C(OH)(CO,C,H-).	$\mathrm{G}_{\bullet}\mathrm{H}_{5}\mathrm{N}(\mathrm{C}_{2}\mathrm{H}_{5})_{2}$	$C[C_6H_4N(CH_3)_2^-p](CO_2CH_3)_2$ $[p\cdot(C_2H_5)_2NC_6H_4]_2(CO_2C_2H_5)_2$	1	POCI			
Note: References 577	Note: References 577-1080 are on pp. 322-331.			; ; ;	V6H5N(V2H5)2	373	321

### REFERENCES TO TABLES I-XX

- 577 Conrad and Bischoff, Ann., 204, 143 (1880). 578 Bischoff and Rach, Ann., 234, 54 (1886). 579 Meyer and Bock, Ann., 347, 93 (1906). 580 Züblin, Ber., 12, 1112 (1879). 581 Funk, Ber., 26, 2568 (1893). 582 Olivier, Rec. trav. chim., 55, 1027 (1036). 583 Crawford, J. Am. Chem. Soc., 56, 139 (1934). 584 Conrad and Guthzeit, Ber., 15, 2841 (1882). 585 Guthzeit and Dressel, Ber., 22, 1413 (1880). 586 Urushibara, Bull. Chem. Soc. Japan, 2, 26 (1927). 587 Coutelle, J. prakt. Chem., [2] 73, 49 (1906). 588 Zelinsky and Doroschewsky, Bcr., 27, 3374 (1894). 589 Dimroth, Ber., 35, 2881 (1902). 590 Ingold and Powell, J. Chem. Soc., 119, 1222 (1921). 591 Hunter, Chem. News, 131, 131 (1925). 592 Conrad, Ann., 204, 127 (1880). 593 Gault and Salomon, Ann. chim. Paris, [10] 2, 133 (1024). 594 Conrad, Ber., 12, 749 (1879). 595 Schey, Rec. trav. chim., 16, 356 (1897). 596 Meunier, Compt. rend., 137, 714 (1903). 597 Daimler, Ann., 249, 173 (1888). 598 Michael, Am. Chem. J., 25, 419 (1901). 599 Joukowsky, J. prakt. Chem., [2] 39, 446 (1889). 600 Lean and Lees, J. Chem. Soc., 71, 1062 (1897). 601 Röder, Ann., 227, 13 (1885). 602 Noves and Kyriakides, J. Am. Chem. Soc., 32, 1057 (1910). 603 Perkin, Ber., 19, 2038 (1886). 604 Perkin, Ber., 17, 54 (1884). 605 Infiesta, Martin, Guzmán, and Alberola, Anales real soc. españ. fís. y quim. Madrid, 47B, 453 (1951) [C. A., 46, 3953 (1952).] 606 Bennett, J. Chem. Soc., 127, 1277 (1925). <sup>607</sup> Leuchs and Gieseler, Ber., 45, 2114 (1912). 608 Ruhemann, Ber., 29, 1016 (1896). 609 Kleber, Ann., 246, 97 (1888). 610 Řeřicha and Protiva, Chem. Listy, 44, 232 (1950) [C. A., 45, 8017 (1951)]. 611 Backer and Toxopéus, Ree. trav. ehim., 45, 895 (1926). 612 Mishin and Poloehanskaya, Colloid J. (U.S.S.R.), 2, 317 (1936) [C. A., 30, 6261 (1936)]. 613 Stiassny, Monatsh. Chem., 12, 589 (1891). 614 Fürth, Monatsh. Chem., 9, 308 (1888). 615 Conrad and Bisehoff, Ber., 13, 595 (1880). 616 Linstead and Rydon, J. Chem. Soc., 1933, 580. 617 Shonle, U.S. pat. 1,842,293 [C. A., 26, 1617 (1932)]. 618 Böeseken and Mass Geesteranus, Ree. trav. chim., 51, 551 (1932). 619 Conrad and Bisehoff, Ann., 204, 166 (1880). 620 Matweeff, J. prakt. Chem., [2] 39, 451 (1889). 621 Hill and Fischer, J. Am. Chem. Soc., 44, 2582 (1922). 622 Favorskaya and Yakovlev, Zhur. Obshchel Khim. (J. Gen. Chem. U.S.S.R.), 22, 122 (1952) [C. A., 46, 11119 (1952)]. 623 Fischer and Bergmann, Ann., 398, 96 (1913).
  - 7897 (1938)].
     Mariella and Raube, Bol. col. quim. Puerto Rico, 8, 24 (1951) [C. A., 46, 4491 (1952)].
     Marburg, Ber., 28, 8 (1895).

624 Venus-Danilova, Zhur. Obshchet Khim. (J. Gen. Chem. U.S.S.R.), 8, 477 (1938) [C. A.,

- 627 Willstätter and Ettlinger, Ann., 326, 91 (1903).
- 628 Willstätter, Ber., 33, 1160 (1900).
- 629 Dutta, Science and Culture India, 5, 560 (1940) [C. A., 34, 6933 (1940)].
- 630 Baeyer, Ann., 278, 88 (1893).
- 631 Perkin, Bcr., 18, 3246 (1885).
- 632 Curtius and Grandel, J. prakt. Chem., [2] 94, 339 (1917).
- 633 Perkin, Ber., 16, 1787 (1883).
- 634 Gault and Salomon, Compt. rend., 174, 754 (1922).
- 635 Biselioff, Ber., 29, 966 (1896).
- 636 Hudlicky, Chem. Listy, 40, 125 (1946) [C. A., 45, 560 (1951)].
- 637 Bua and Tibaldi, Farm. sci. c tec. Pavia, 6, 448 (1951) [C. A., 46, 8004 (1952)].
- 638 Perkin and Simonsen, J. Chem. Soc., 91, 840 (1907).
- 639 Perkin and Simonsen, J. Chem. Soc., 91, 816 (1907).
- 640 Adams and Marvel, J. Am. Chem. Soc., 42, 310 (1920).
- 641 Armendt and Adams, J. Am. Chem. Soc., 52, 1289 (1930).
- 642 Bentley and Perkin, J. Chem. Soc., 73, 45 (1898).
- 643 Ställberg-Stenhagen, Arkiv Kemi, Mineral. Geol., A19, No. 28, 9 (1945) [C. A., 41, 1604 (1947)].
- 644 Chichibabin and Katznolson, Bull. acad. sci., U.R.S.S., Classe sci. math. nat., 1933, 267 [C. A., 27, 3698 (1933)].
- 645 Katznolson and Kondakova, Compt. rend. acad. sci. U.R.S.S. [N.S.], 2, 21 (1934) [C. A., 28, 5042 (1934)].
  - 646 Prelog and Božičovič, Ber., 72, 1103 (1939).
  - 647 Linstead and Rydon, J. Chem. Soc., 1934, 1995.
  - <sup>648</sup> Eccott and Linstead, J. Chem. Soc., 1929, 2153.
  - 649 Arvin and Adams, J. Am. Chem. Soc., 50, 1983 (1928).
  - 850 Stauss, Ber., 27, 1228 (1894).
  - 651 Holferich and Speidel, Bcr., 54, 2634 (1921).
- 652 Tatevosyan and Tuteryan, Bull. Acad. Sci. Armenian U.S.S.R., 1944, No. 5, 29 [C A., 40, 3404 (1946)].
  - 653 Michael, Bcr., 38, 3217 (1905).
  - 654 Paal, Ber., 39, 1436 (1906).
  - 655 Bisehoff, Ann., 214, 38 (1882).
- 656 Franke, Kroupa, Schweitzer, Winischofer, Klein-Lohr, Just, Hackl, Reyhor, and Bader, Monatsch. Chem., 69, 167 (1936).
  - 657 Curtius, Sieber, Nadenheim, Hambseli, and Ritter, J. prakt. Chem., [2] 125, 152 (1930).
  - 658 Paal and Hoffmann, Ber., 23, 1495 (1890).
  - 659 Dewael and Weckering, Bull. soc. chim. Belg., 33, 495 (1924) [C. A., 19, 463 (1925)].
  - 660 Bergmann and Sprinzak, Helv. Chim. Acta, 20, 590 (1937).
  - 661 Gaubert, Linstead, and Rydon, J. Chem. Soc., 1937, 1971.
  - 662 Schmid, Helv. Chim. Acta, 27, 127 (1944).
  - <sup>663</sup> Allais and Mathiou, Ann. pharm. franç., 9, 275 (1951) [C. A., 45, 10499 (1951)].
  - Bohrens, Corse, Huff, Jones, Soper, and Whitehead, J. Biol. Chem., 175, 771 (1948).
  - 665 Colman and Perkin, J. Chem. Soc., 53, 185 (1888).
  - 666 Staudinger, Kreis, and Schilt, Helv. Chim. Acta, 5, 743 (1922).
  - 667 Ssolonina, J. Russ. Phys. Chem. Soc., 33, 734 (1902) (Chem. Zentr., 1902, I, 629).
  - 666 Karrer, Keller, and Usteri, Helv. Chim. Acta, 27, 237 (1944).
  - 669 Bischoff, Ann., 214, 53 (1882).
  - 670 Emery, Ber., 24, 282 (1891).
  - 671 Alekseeva and Mezhov, Zhur. Obshchel Khim. (J. Gen. Chem. U.S.S.R.), 22, 1813 (1952)
- [C. A., 47, 5357 (1953)].
  - 672 Heinko and Perkin, J. Chem. Soc., 69, 1506 (1896).
  - 673 Conrad and Guthzeit, Ber., 17, 1185 (1884).
  - <sup>674</sup> Goldshmiodt and Knöpfer, Monatsh. Chem., 17, 506 (1896).
  - 676 Bischoff, Ber., 29, 1276 (1896).
  - 676 Verwoy, Ber., 29, 1996 (1896).

. L

- 677 Ipatieff, Germain, and Pincs, Bull. soc. chim. France, 1951, 259.
- 678 von Braun, Münch, and Deusser, Ann., 465, 52 (1928).
- 679 Buu-Hoi and Cagniant, Bull. soc. chim. France, [5] 10, 477 (1943).
- 680 Arvin and Adams, J. Am. Chem. Soc., 49, 2940 (1927).
- 681 Moffett, Org. Syntheses, 32, 52 (1952).
- 682 Barger. Robinson, and Smith, J. Chem. Soc., 1937, 718.
- 683 Schudel and Rice, U.S. pat. 2,522,966 [C. A., 45, 6223 (1951)].
- 684 Chargaff, Ber., 65, 745 (1932).
- 685 Asano and Yamakawa, J. Pharm. Soc. Japan, 70, 474 (1950) [C. A., 45, 5617 (1951)].
- 686 Ficser, Berliner, Bondhus, Chang, Dauben, Ettlinger, Fawaz, Fields, Heidelberger, Heymann, Vaughan, Wilson, Wilson, Wu, Loffler, Hamlin, Matson, Moore, and Zaugg, J. Am. Chem. Soc., 70, 3174 (1948).
  - <sup>687</sup> Motti, Anesthésie et analgésie, 2, 52 (1936) [C. A., 31, 3010 (1937)].
  - 558 Fourneau and Matti, J. pharm. chim., [8] 14, 513 (1931) [C. A., 28, 3073 (1932).
  - 889 Strukov, Zhur. Obshchol Khim. (J. Gen. Chem. U.S.S.R.), 22, 521 (1952) [C. A., 47, 2755 (1953)].
    - <sup>690</sup> Whitmore, Jones, and Noll, U.S. pat. 2,161,213 [C. A., 33, 7313 (1939)].
    - 691 Letsinger and Schnizer, J. Org. Chem., 16, 704 (1951).
    - 692 Howton and Davis, J. Org. Chem., 16, 1405 (1951).
    - 693 Stoll and Bolle, Helv. Chim. Acta, 21, 1547 (1938).
    - 694 Pudovik and Arbuzov, Bull. acad. sci. U.R.S.S., Classe sci. chim., 1947, 501 [C, A., 42, 1887 (1948)].
      - 695 Newman and Wotiz, J. Am. Chem. Soc., 71, 1292 (1949).
      - 696 Freer and Perkin, J. Chem. Soc., 53, 202 (1888).
      - 697 Ipatiew, J. Russ. Phys. Chem. Soc., 31, 349 (1899) (Chem. Zentr., 1899 II, 25).
      - 698 Cheney and Pioning, J. Am. Chem. Soc., 67, 2213 (1945).
      - 699 Mannich and Margotte, Ber., 68, 273 (1935).
      - 700 Cason, Wallcave, and Whitside, J. Org. Chem., 14, 37 (1949).
      - 701 Barnstein, Ann., 242, 126 (1887).
      - 702 Leukart, Ber., 18, 2344 (1885).
      - 703 Buchner and Witter, Ann., 284, 225 (1895).
      - 704 Hiers and Adams, J. Am. Chem. Soc., 48, 2385 (1926).
      - 705 Ishiwata and Nozaki, J. Pharm. Soc. Japan, 71, 1261 (1951) [C. A., 46, 5590 (1952)].
      - 706 Coffey, Rec. trav. chim., 42, 387 (1923).
      - 707 Kôtz and Hoffman, J. prakt. Chem., [2] 110, 101 (1925).
      - <sup>708</sup> Blicke, U.S. pat. 2,533,084 [C. A., 45, 3423 (1951)].
      - 709 Blicke, U.S. pat. 2,541,024 [C. A., 46, 537 (1952)].
      - 710 Koelsch, J. Am. Chem. Soc., 66, 1611 (1944.)
      - 711 Jackson and Soch, Am. Chem. J., 18, 133 (1896).
      - 712 Borsche, Stackmann, and Makaroff-Somljanski, Bcr., 49, 2222 (1916).
      - 713 Sen and Bhargava, J. Indian Chem. Soc., 25, 538 (1948).
      - 714 Borsche and Trautner, Ann., 447, 1 (1926).
      - 715 Sen and Bhargava, J. Indian Chem. Soc., 24, 371 (1947).
      - 716 Prelog and Schönbaum, Ann., 545, 256 (1940).
      - 717 Ames, Bowman, and Mason, J. Chem. Soc., 1950, 174.
      - 718 Kondo and Suzuki, Ber., 69, 2459 (1936).
      - 719 Bondar and Zelinskii, Doklady Akad, Nauk S.S.S.R., 72, 881 (1950) [C. A., 44, 9365] (1950)].
        - 720 Staudinger and Ruzicka, Helv. Chim. Acta, 7, 245 (1924).
        - 721 Huber, Clinton, Buck, Lawson, and Beal, J. Am. Chem. Soc., 67, 1148 (1945).
        - 722 Conrad and Bischoff, Ann., 214, 68 (1882).
        - 723 Conrad and Guthzeit, Ber., 17, 2285 (1884).
        - 724 Burschkies and Scholl, Arch. Pharm., 281, 328 (1943).
        - 725 Yohe and Adams, J. Am. Chem. Soc., 50, 1503 (1928).
        - 726 Burschkies and Scholl, Chem. Ber., 82, 224 (1949).
        - 727 Adams, Noller, and Arvin, U.S. pat. 1,678,175 [C. A., 22, 3491 (1928)].

- <sup>728</sup> Szarvasi, Dupont, and Dulou, Chimie & industrie, 62, 143 (1949) [C.A., 44, 5345 (1950)].
- 729 Zelinsky and Alexandrow, Ber., 34, 3885 (1902).
- 730 Mousseron, Granger, and Winternitz, Compt. rend., 217, 246 (1943).
- 731 Haller and Barthe, Ann. chim. Paris, [6] 18, 28 (1889).
- 732 Conrad, Ann., 204, 174 (1880).
- 733 Doebner and Kersten, Ber., 38, 2737 (1905).
- 734 Leuchs and Radulescu, Ber., 45, 189 (1912).
- 735 Gardner and Rydon, J. Chem. Soc., 1938, 42.
- 736 Barnes and Gordon, J. Am. Chem. Soc., 71, 2644 (1949).
- 737 Dankova, Bokova, Preobrazhenskii, Petrushchenko, Il'shtein, and Stivetsov, Zhur. Obshchel Khim. (J. Gen. Chem. U.S.S.R.), 21, 787 (1951) [C. A., 45, 9517 (1951)].
  - <sup>738</sup> von Braun and Nelles, Ber., 66, 1464 (1933).
  - 739 Leuchs and von Katinszky, Ber., 55, 710 (1922).
  - 740 Lellmann and Schleich, Ber., 20, 434 (1887).
  - 741 Reissert, Ber., 27, 2244 (1894).
  - 742 Radulescu, Bul. Soc. Stiinte Cluj, 1, 306 (1922) [C. A., 18, 1285 (1924)].
  - 743 von Braun, Anton, and May, Ber., 70, 1250 (1937).
  - 744 Clutterbuck, Raistrick, and Rintoul, Trans. Roy. Soc., B220, 301 (1931).
  - 745 Conrad and Bischoff, Ann., 204, 162 (1880).
  - 746 Dickman, Rev. fac. sci. univ. Istanbul, 15A, 108 (1950) [C. A., 45, 6154 (1951)].
  - 747 Levene and Kuna, J. Biol. Chem., 140, 255 (1941).
  - <sup>748</sup> Suzuki, J. Pharm. Soc. Japan, 56, 860 (1936) [C. A., 33, 130 (1939)].
- 749 Weizmann, Bergmann, and Haskelberg, Chemistry & Industry, 15, 587 (1937) [C. A., 31, 7407 (1937)].
  - 750 Dutta, J. Indian Chem. Soc., 19, 79 (1942).
- 751 Matsui and Hirase, J. Chem. Soc. Japan, Pure Chem. Sect., 71, 426 (1950) [C. A., 45, 8984 (1951)].
  - 752 Bischoff, Ber., 29, 1504 (1896).
  - 753 Bernton, Ing, and Perkin, J. Chem. Soc., 125, 1492 (1924).
  - 754 Coleman, Callen, and Dornfeld, J. Am. Chem. Soc., 68, 1101 (1946).
  - 755 Blicke and Contollela, J. Am. Chem. Soc., 60, 2923 (1938).
  - 756 Rupo and Wolfsleben, Ann., 395, 111 (1913).
  - <sup>757</sup> Leuchs and Reinhart, Ber., 57, 1208 (1924).
  - 758 Bentley, Haworth, and Perkin, J. Chem. Soc., 69, 161 (1896).
  - 759 Wessely and Wang, Ber., 73, 19 (1940).
  - 760 Hoch, Compt. rend., 192, 1464 (1931).
  - 761 Clemo and Swan, J. Chem. Soc., 1949, 487.
  - 762 Curtius and Marangolo, J. prakt. Chem., [2] 94, 331 (1917).
  - 763 Asano and Kawasaki, J. Pharm. Soc. Japan, 70, 480 (1950) [C. A., 45, 5661 (1951)].
  - 764 Chakravarti and Rao, J. Chem. Soc., 1938, 172.
  - 765 Kues and Paul, Ber., 18, 3323 (1885).
  - 766 Bisehoff, Ber., 16, 1044 (1883).
  - 767 von Baeyer and Perkin, Ber., 17, 122 (1884).
  - 768 Leuchs and Sander, Ber., 58, 2200 (1925).
  - 769 von Braun, Teuffert, and Manz, Ber., 62, 235 (1929).
  - 770 Jones and Pyman, J. Chem. Soc., 127, 2588 (1925).
  - <sup>771</sup> Przewalski, J. Russ. Phys. Chem. Soc., 49, 567 (1917) (Chem. Zentr., 1923, III, 664).
  - 772 Günther, Ber., 31, 2134 (1898).
  - 773 Gabriel, Ber., 25, 415 (1892).
  - 774 Granger, Ber., 28, 1197 (1895).
  - 775 Prelog, Heimbech, and Seiwerth, Ber., 72, 1319 (1939).
  - 776 Merchant, Wickert, and Marvel, J. Am. Chem. Soc., 49, 1828 (1927).
  - <sup>777</sup> Carter, J. Am. Chem. Soc., 50, 1967 (1928).
  - <sup>776</sup> Wagner-Jauregg, Arnold, and Hüter, Ber., 75, 1293 (1942).

  - 779 Kadesch, J. Am. Chem. Soc., 66, 1207 (1944).
  - <sup>780</sup> Emerson and Heimsch, J. Am. Chem. Soc., 72, 5152 (1950).

781 Liebermann, Ber., 32, 260 (1899). 782 Cagniant, Bull. soc. chim. France, 1949, 382. 783 Buu-Hoi and Cagniant, Ber., 76, 689 (1943). 784 Prout, Cason, and Ingersoll, J. Am. Chem. Soc., 69, 1233 (1947). 785 Forster and Cardwell, J. Chem. Soc., 103, 1338 (1913). 786 Mukherjee, J. Indian Chem. Soc., 24, 425 (1947). 787 Treibs and Mayer, Chem. Ber., 85, 612 (1952). 788 Ziegler and Weber, Ann., 512, 164 (1934). 789 Perkin and Robinson, J. Chem. Soc., 119, 1392 (1921). 790 Quadrat-i-Khuda and Mukherjee, J. Indian Chem. Soc., 16, 532 (1939). 791 Nenitzeseu and Gavat, Ann., 519, 260 (1935). 792 Marvel, MacCorquodale, Kendall, and Lazier, J. Am. Chem. Soc., 48, 2838 (1924). 793 Prelog, Šoštarič, and Guštak, Ann., 545, 247 (1940). 794 Kögl, Verbeck, Erxleben, and Borg, Hoppe-Scyler's Z. physiol. Chem., 279, 121 (1943). 785 Colonge and Pichat, Bull. soc. chim. France, 1949, 177. 796 van der Zandon, de Vries, and Westerhof, Rec. trav. chim., 62, 383 (1943). 797 Smith and Agre, J. Am. Chem. Soc., 60, 652 (1938). 798 Guha and Bhattacharyya, J. Indian Chem. Soc., 21, 271 (1944). 799 Clemo, Groves, Munday, and Swan, J. Chem. Soc., 1951, 863. 800 Buchnor and Dessauer, Ber., 25, 1153 (1892). 801 Hoffmann, Ber., 34, 1558 (1901). 802 Lovene, West, Allen, and Van der Scheer, J. Biol. Chem., 23, 71 (1915). 803 Gaubert, Linstead, and Rydon, J. Chem. Soc., 1937, 1974. 804 Genslor, Behrmann, and Thomas, J. Am. Chem. Soc., 73, 1071 (1951). 805 Harmon and Marvol, J. Am. Chem. Soc., 54, 2515 (1932). 806 Tsatsas, Ann. chim. Paris, [12] 1, 342 (1946). 807 Clomo, Haworth, and Walton, J. Chem. Soc., 1929, 2368. 808 Whittleston, J. Am. Chem. Soc., 59, 825 (1937). 809 Aitken, Badger, and Cook, J. Chem. Soc., 1950, 331. 810 Fuson, House, and Molby, J. Am. Chem. Soc., 75, 5952 (1953). 811 Gabriel, Ber., 23, 1767 (1890). 812 Kipping and Perkin, J. Chem. Soc., 57, 304 (1890). 813 Haerdi and Thorpe, J. Chem. Soc., 127, 1237 (1925). 814 Crossley and Perkin, J. Chem. Soc., 85, 987 (1894). 815 Lehman, Thompson, and Marvel, J. Am. Chem. Soc., 55, 1977 (1933). 816 Buckle, Pattison, and Saunders, J. Chem. Soc., 1949, 1471. 817 Tatevosyan and Babayan, Zhur. Obshchel Khim. (J. Gen. Chem. U.S.S.R.), 22, 1421 (1952) [C. A., 47, 4869 (1953)]. 818 Fischer and Neber, Ann., 496, 1 (1932). 819 Bachmann, Gregg, and Pratt, J. Am. Chem. Soc., 65, 2314 (1943). 820 Ansell and Hey, J. Chem. Soc., 1950, 1683. 821 Buu-Hoi and Cagniant, Rev. sci., 80, 271 (1942) [C. A., 39, 3275 (1945)]. 822 Billeter and Miescher, Helv. Chim. Acta., 29, 859 (1946). 823 Lecoeq and Buu-Hoi, Compt. rend., 224, 658 (1947). 824 Campbell, Corrigan, and Campbell, J. Org. Chem., 16, 1712 (1951). 825 Bachmann and Sheehan, J. Am. Chem. Soc., 63, 204 (1941). 826 Kalopissis and Gault, Compt. rend., 231, 1310 (1950). 827 Buu-Hoi and Cagniant, Bull. soc. chim. France, [5] 11, 349 (1944). 828 Koelsch, J. Am. Chem. Soc., 65, 2460 (1943). 829 Holmberg, Acta Acad. Aboensis Math. et Phys., 16, 138 (1948) [C. A., 45, 558 (1951)]. 830 von Braun and Manz, Ann., 468, 258 (1929). 831 Cohen, Cook, and Hewett, J. Chem. Soc., 1936, 52. 832 Smith and Lo, J. Am. Chem. Soc., 70, 2215 (1948). 833 Bachmann and Sheehan, J. Am. Chem. Soc., 62, 2687 (1940). 834 Wittig and Leo, Ber., 62, 1405 (1929).

835 Buu-Hoï and Cagniant, Compt. rend., 214, 493 (1942).

- 836 Karrer, Favarger, Merz, and Milhaud, Helr. Chim. Acta, 31, 1505 (1948).
- 837 Dietrich and Lederer, Compt. rend., 234, 637 (1952).
- 858 Short and Wang, J. Chem. Soc., 1950, 991.
- 859 Wilds and Beck, J. Am. Chem. Soc., 66, 1688 (1944).
- 840 Phillips and Mumford, J. Chem. Soc., 1931, 1732.
- 841 Standinger, Bier, and Lorentz, Makromol. Chem., 3, 251 (1949) [C. A., 44, 2443 (1950)].
- 842 Guthzeit, Ann., 206, 351 (1881).
- <sup>843</sup> van Loon and van der Linden, Rec. trnv. chim., 71, 292 (1952).
- 844 Toyama and Yamamoto, J. Chem. Soc. Japan, Pure Chem. Sect., 72, 619 (1951) [C. A., 47, 1591 (1953)].
  - 845 Raplinel and Sondheimer, J. Chem. Soc., 1950, 2100.
  - 846 Rapinel and Southeimer, Nature, 165, 235 (1950).
  - 847 Stanley and Adams, J. Am. Chem. Soc., 51, 1515 (1929).
  - 848 Bachmann and Carmack, J. Am. Chem. Soc., 63, 2494 (1941).
  - 819 Figser and Chamberlin, J. Am. Chem. Soc., 70, 71 (1948).
  - 850 Van Dyke and Adams, J. Am. Chem. Soc., 48, 2393 (1926).
  - 851 Henderson, J. Chem. Soc., 51, 224 (1887).
- 852 Breitner, Med. u. Chem. Abhandl. med. chem. Forschungsstätten I.G. Farbenind., 4, 317 (1942) [C. A., 38, 4953 (1944)].
  - 853 Hale, Lycan, and Adams, J. Am. Chem. Soc., 52, 4536 (1930).
  - 854 Levene and Taylor, J. Biol. Chem., 52, 227 (1922).
  - 855 Polgar, Robinson, and Scijo, J. Chem. Soc., 1949, 1545.
  - 856 David, Polgar, and Robinson, J. Chem. Soc., 1949, 1541.
  - 857 Conrad and Guthzeit, Ann., 214, 76 (1882).
  - 858 Locquin and Cerchez, Compt. rend., 186, 1360 (1928).
  - 859 Cereliez, Bull. soc. chim. France, [4] 47, 1381 (1930).
  - 860 J. Shapira and K. Dittmer, to be published.
  - 861 Koštiř and Král, Chem. Listy, 43, 37 (1949) [C. A., 45, 562 (1951)].
- 862 Capková-Jirků, Koštiř, and Vondráček, Chem. Listy, 44, 114 (1950) [C. A., 45, 7962 (1951)].
  - 863 J. S. Meek and S. Minkowitz, to be published.
  - 854 J. S. Meek and J. W. Rowe, to be published.
  - 865 Vejdělek and Protiva, Chem. Listy, 45, 44 (1951) [C. A., 45, 9011 (1951)].
  - 866 Goldsmith and Tishler, J. Am. Chem. Soc., 68, 144 (1946).
  - 867 Warner and Moe, Brit. pat. 658,413 [C. A., 46, 9588 (1952)].
  - 868 Rinderknecht and Niemann, J. Am. Chem. Soc., 73, 4259 (1951).
  - 869 Dittmer, Herz, and Chambers, J. Biol. Chem., 166, 541 (1946).
  - 870 Dittmer, Martin, Herz, and Cristol, J. Am. Chem. Soc., 71, 1201 (1949).
  - 871 Elks, Elliott, and Hems, J. Chem. Soc., 1944, 626.
  - 872 Auwers and Thorpe, Ann., 285, 310 (1895).
  - 873 Adams and Rogers, J. Am. Chem. Soc., 63, 228 (1941).
  - 874 Kitzing, Ber., 27, 1578 (1894).
  - 875 Kobayasi, Ann., 536, 143 (1938).
- 876 Ställberg-Stenhagen, Arkiv Kemi, Mineral. Geol., A23, No. 15, 14 (1946) [C. A., 41, 5443 (1947)].
  - 877 Bischoff and Voit, Ber., 23, 639 (1890).
  - 878 Cagniant, Compt. rend., 232, 734 (1951).
- 879 Cavanna and Ställberg-Stenhagen, Atti accad. nazl. Lincei, Mem. Classe eci. fie. mat. e nat., [8] 3, 31 (1950) [C. A., 45, 9470 (1951)].
  - 880 Noyes, Ber., 33, 54 (1900).
  - 881 Adkins and Davis, J. Am. Chem. Soc., 71, 2955 (1949).
- AGKINS and Davis, J. Am. Oscario, Mineral. Geol., 26A, No. 12, 28 (1948) [C. A., 43, 882 Ställberg-Stenhagen, Arkiv Kemi, Mineral. Geol., 26A, No. 12, 28 (1948) [C. A., 43, 6160 (1949)].
  - 883 Ruzieka and Hosking, Helv. Chim. Acta, 13, 1402 (1930).
  - 884 Robinson and Suginome, J. Chem. Soc., 1932, 304.
  - 885 Fieser and Novello, J. Am. Chem. Soc., 62, 1855 (1940).

886 Vargha and Gyorffy, Magyar Chem. Folyóirat, 50, 6 (1944) [C. A., 42, 1219 (1948)]. 887 Greer and Adams, J. Am. Chem. Soc., 52, 2540 (1930). 888 Stanley, Jay, and Adams, J. Am. Chem. Soc., 51, 1261 (1929). 389 Fernholz and Finkelstein, J. Am. Chem. Soc., 60, 2402 (1938). 890 Jones, U.S. pat. 2,363,003 [C. A., 39, 3791 (1945)]. 891 Paal and Kühn, Ber., 41, 51 (1908). 892 Raper, J. Chem. Soc., 91, 1837 (1907). 893 Walter, U.S. pat. 2,354,231 [C. A., 39, 1416 (1945)]. 894 Paal and Kühn, Ber., 41, 58 (1908). 895 Shonlo, U.S. pat. 1,813,867 [C. A., 25, 5249 (1931)]. 896 Huang-Minlon, Contribs. Biol. Lab. Sci. Soc. China, Zool. Ser., 15, 17 (1940) [C. A., 36, 80 (1942)]. 897 Morren, Dony, and Levis, J. pharm. Belg., 7, 65 (1952) [C. A., 47, 5895 (1953)]. 898 Bywater, U.S. pat. 2,200,538 [C. A., 34, 6019 (1940)]. 899 Walter and Goodson, U.S. pat. 2,354,234. [C. A., 39, 1417 (1945)]. <sup>900</sup> Plati, Strain, and Warren, J. Am. Chem. Soc., 65, 1273 (1943). 901 Hsuoh and Marvel, J. Am. Chem. Soc., 50, 855 (1928). 302 Adams, Stanloy, Ford, and Peterson, J. Am. Chem. Soc., 49, 2934 (1927). 903 Lévy, Compt. rend., 202, 1679 (1936). 804 Dittrich and Paal, Ber., 21, 3451 (1888). 905 Cocker, Cross, Fateen, Lipman, Stuart, Thompson, and Whyte, J. Chem. Soc., 1950, 1781. 906 Brunner and Wiedemann, Monatsh. Chem., 68, 438 (1935). 907 Meyer, Compt. rend., 203, 1074 (1936). 908 Meyer, Compt. rend., 203, 1370 (1936). 909 Kondakova and Katsnel'son, Compt. rend. acad. sci. (U.R.S.S.), 18, 271 (1938) [C. A., 32, 4523 (1938)]. 910 Work, J. Chem. Soc., 1946, 197. 911 Kolloff, Hunter, Woodruff, and Moffett, J. Am. Chem. Soc., 70, 3862 (1948). 912 Staudinger, Muntwyler, Ruzieka, and Seibt, Helv. Chim. Acta, 7, 390 (1924). 913 Pratt and Archer, J. Am. Chem. Soc., 70, 4065 (1948). 914 Buu-Hoi and Cagniant, Hoppe-Seyler's Z. physiol. Chcm., 279, 76 (1943). 915 Hildebrandt and Leube, Ger. pat. 494,320 [C. A., 24, 2756 (1930)]. 816 Tatevosyan and Melikyan, Zhur. Obshchei Khim. (J. Gen. Chem. U.S.S.R.), 17, 975 (1947) [C. A., 42, 1566 (1948)]. 917 Tatevosyan and Nikogosyan, Proc. Acad. Sci. Armenian S.S.R., 1945, III, 15 [C. A., 40, 3397 (1946)]. <sup>918</sup> Hall, Mahboob, and Turner, J. Chem. Soc., 1952, 1956. 919 von Braun and Kröper, Ber., 62, 2880 (1929). 920 Browning, Woodrow, and Adams, J. Am. Chem. Soc., 52, 1281 (1930). 921 Waltz, Ann., 214, 58 (1882). 922 Bischoff, Ann., 214, 61 (1882). 923 Bischoff and Mintz, Ber., 23, 653 (1890). 924 Leonard, J. Am. Chem. Soc., 74, 2915 (1952). 925 von Braun and Fischer, Ber., 66, 101 (1933). 926 von Braun and Kurtz, Ber., 70, 1224 (1937). 927 Moffott, Hart, and Hoehn, J. Am. Chem. Soc., 69, 1849 (1947). 928 Arvin and Adams, J. Am. Chem. Soc., 50, 1790 (1928). 929 Davies and Adams, J. Am. Chem. Soc., 50, 2297 (1928). 930 Lcder-Pakkendorf, Compt. rend. acad. sci. (U.R.S.S.), 31, 757 (1941) [C. A., 37, 871 (1943)1. 931 McElvain and Laughton, J. Am. Chem. Soc., 73, 448 (1951). 932 Roberts and Selby, J. Chem. Soc., 1951, 2335. 933 Miescher and Hoffmann, Helv. Chim. Acta, 24, 458 (1941). 934 Jackman, Bergman, and Archer, J. Am. Chem. Soc., 70, 497 (1948).

935 Buu-Hoi, Cagniant, and Mentzer, Bull. soc. chim. France, [5] 11, 127 (1944).

\*36 Charpentier, U.S. pat. 2,570,024 [C. A., 46, 3562 (1952)]. 937 Adams, Van Duuren, and Brown, J. Am. Chem. Soc., 74, 5608 (1952). 938 Geissman and Tulagin, J. Am. Chem. Soc., 66, 719 (1944). 939 Conrad and Bischoff, Ann., 264, 177 (1880). 940 Simonsen, J. Chem. Soc., 117, 564 (1920). 941 Ingold and Rogers, J. Chem. Soc., 1935, 717. 942 Nnik, Shah, and Nargund, J. Univ. Bombay, 19, Sect. A, Pt. 3, Sci. No. 28, 19 (1950) [C. A., 46, 11124 (1952)].945 von Braun and Hamann, Ber., 65, 1580 (1932). 944 Duff and Ingold, J. Chem. Soc., 1934, 87. 945 von Braun, Manz, and Reinsch, Ann., 468, 277 (1929). 946 Bergmann, J. Org. Chem., 4, 1 (1939). 947 Ford and Adams, J. Am. Chem. Soc., 52, 1259 (1930). 946 Tatevosyan and Vardanyan, Proc. Acad. Sci. Armenian S.S.R., 4, No. 3, 71 (1946) [C. A., 41, 432 (1947)]. 949 Buchta and Dauner, Chem. Ber., 81, 247 (1948). 950 Jacques and Horean, Bull. soc. chim. France, 1956, 512. 951 von Braun and Schattner, Ber., 74, 22 (1941). 952 Cope, Meili and MacDowell, J. Am. Chem. Soc., 78, 2551 (1956). 953 Bachmann and Anderson, J. Org. Chem., 13, 297 (1948). 954 Kohler, Am. Chem. J., 34, 132 (1905). 955 Cope, Field, MacDowell, and Wright, J. Am. Chem. Soc., 78, 2547 (1956). 956 Kohler, Am. Chem. J., 46, 485 (1911). 957 Staudinger and Kern, Ber., 66, 373 (1933). 958 Kohler and Conant, J. Am. Chem. Soc., 39, 1699 (1917). 959 Perkin, J. Chem. Soc., 87, 358 (1905). 950 Gregory and Perkin, J. Chem. Soc., 83, 780 (1903). 961 Kon, Linstead, and Maclennan, J. Chem. Soc., 1932, 2452. 962 Henry, Compt. rend., 104, 1618 (1887). 963 Henry, Jahresber., 1889, 637. 964 Urushibara, Bull. Chem. Soc. Japan, 2, 236 (1927). 965 Errern, Gazz. chim. ital., 27, 11, 393 (1897). 966 Ruhemann and Browning, J. Chem. Soc., 73, 280 (1898). 967 Errern, Ber., 31, 1241 (1898). 968 Hadley, J. Am. Chem. Soc., 34, 923 (1912). 969 Földi, Fodor, Demjen, Szekeres, and Halmos, Ber., 75, 755 (1942). 970 Dai Nippon Celluloid Co., Jap. pat. 157,332 [C. A., 43, 9475 (1949)]. 971 Fischer and Brieger, Ber., 48, 1517 (1915). 972 Fischer and Brieger, Chem. Zentr., 86, II, 222 (1915). 973 Darapsky, J. prakt. Chem. [2], 146, 250 (1936). 974 Barthe, Ann. chim. Paris, [6] 27, 239 (1892). 975 Freylon, Ann. chim. Paris, [8] 19, 562 (1910). 976 I.G. Farbenindustric, A.-G., Swiss pat. 116,292 [Chem. Zentr., 97, II, 2850 (1926)]. 977 Haller and Barthe, Compt. rend., 106, 1413 (1888). 978 Curtius and Wirbatz, J. prakt. Chem., [2] 125, 267 (1930). 970 Perkin, J. Chem. Soc., 85, 416 (1904). 980 Wren and Haller, J. Chem. Soc., 1937, 230. 981 Verkade and Hartman, Rec. trav. chim., 52, 945 (1933). 982 Gagnon, Gaudry, and King, J. Chem. Soc., 1944, 13. <sup>973</sup> Volwiler and Tabern, J. Am. Chem. Soc., 58, 1352 (1936). 984 Bone and Sprankling, J. Chem. Soc., 77, 654 (1900). 985 Bone and Sprankling, J. Chem. Soc., 77, 1298 (1900). 986 Liebermann, Ber., 32, 916 (1899). 987 Hellerman, J. Am. Chem. Soc., 49, 1735 (1927).

988 Zelinsky, Ber., 22, 2823 (1889).

989 Bone and Perkin, J. Chem. Soc., 67, 416 (1895).

- <sup>1043</sup> Vasiliu, Dumitrascu, and Vulcan, Soc. Chim. România Scct. Românâ Stiinte, Bul. Chim. Pura Apl., [2] 3A, 54 (1941-1942) [C. A., 38, 5493 (1944).]
  - 1044 Panizzon, Helv. Chim. Acta, 27, 1748 (1944) [C. A., 40, 3117 (1946)].
  - 1045 Vasiliu, Bul. Soc. Chim. România, 19A, 75 (1937) [C. A., 33, 4207 (1939)].
- <sup>1046</sup> Venus-Danilova and Bol'shukin, Zhur. Obshchel. Khim. (J. Gen. Chem. U.S.S.R.), 7, 2823 (1937) [C. A., 32, 2925 (1938)].
  - 1047 Upson and Thompson, J. Am. Chem. Soc., 44, 181 (1922).
  - 1048 Mcycr, Ber., 21, 1306 (1888).
  - 1049 Walters and McElvain, J. Am. Chem. Soc., 55, 4625 (1933).
  - 1050 Bockmühl and Ehrhardt, Ger. pat. 473,329. [Chem. Zentr., 100 (11), 218 (1929)].
  - 1051 Bockmühl and Schwarz, U.S. pat. 1,482,343. [Chem. Zentr., 95 (II), 1631 (1924)].
  - <sup>1052</sup> Rising and Lowe, J. Am. Chem. Soc., 52, 2524 (1930).
  - 1053 Salmon-Legagneur and Neveu, Compt. rend., 234, 1060 (1952).
  - 1054 Vasiliu and Radvan, Bul. Soc. Chim. România, 20A, 243 (1938) [C. A., 34, 4058 (1940)].
  - 1055 Blicke, U.S. pat. 2,542,466 [C. A., 45, 7141 (1951).
  - 1056 Iwaya and Yoshida, J. Pharm. Soc. Japan, 71, 1454 (1951) [C. A., 46, 7065 (1952)].
  - 1057 Dupré, Elks, Hems, Speyer, and Evans, J. Chem. Soc., 1949, 500.
  - 1058 Salmon-Legagneur, Bull. soc. chim. France, 1952, 580.
  - 1059 Easton, Reiff, Svarnas, and Fish, J. Am. Chem. Soc., 74, 260 (1952).
  - <sup>1060</sup> Morrison and Rinderknecht, J. Chem. Soc., 1950, 1478.
  - 1061 Ofner and Walton, J. Chem. Soc., 1950, 2158.
  - 1062 Ofner, Thorp, and Walton, Nature, 163, 479 (1949).
  - Wilson, J. Chem. Soc., 1952, 3524.
     Löwenbein and Gagarin, Ber., 58, 2643 (1925).
  - 1065 Wojeik and Adkins, J. Am. Chem. Soc., 56, 2424 (1934).
  - 1066 Vogel, J. Chem. Soc., 1927, 1985.
  - 1067 Cope and Hardy, J. Am. Chem. Soc., 62, 3319 (1940).
  - 1068 Adkins and Billica, J. Am. Chem. Soc., 70, 695 (1948).
  - 1069 Hinz, Meyer, and Schücking, Bcr., 76, 676 (1943).
  - 1070 Clemo, Fletcher, Fulton, and Raper, J. Chem. Soc., 1950, 1140.
  - 1071 Horeau and Jacques, Compt. rend., 228, 1873 (1949).
  - <sup>1072</sup> Baltzly and Buck, J. Am. Chem. Soc., 62, 161 (1940).
  - 1073 Alexander and Cope, Org. Syntheses, 26, 31 (1946).
  - 1074 Holmberg, Acta Chem. Scand., 6, 421 (1952) [C. A., 47, 2141 (1953)].
  - <sup>1075</sup> Prout, J. Am. Chem. Soc., 74, 5915 (1952).
  - 1076 Birch and Robinson, J. Chem. Soc., 1943, 501.
  - 1077 Barltrop and Nicholson, J. Chem. Soc., 1951, 2524.
  - <sup>1078</sup> Ando, J. Chem. Soc. Japan, 57, 1351 (1936) [C. A., 31, 2596 (1937)].
  - 1079 Guyot and Esteva, Compt. rend., 148, 564 (1909).
  - 1080 Guyot and Esteva, Compt. rend., 148, 719 (1909).

#### CHAPTER 5

### THE REACTION OF HALOGENS WITH SILVER SALTS OF CARBOXYLIC ACIDS

#### C. V. Wilson

#### Eastman Kodak Company

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#### INTRODUCTION

The action of halogens with *dry* metallic salts, particularly silver salts of carboxylic acids has merited earlier reviews. 1-2a It has been pointed out that the halogen used, the ratio of silver salt to halogen, and the presence or absence of other active materials, such as olefins, acetylenes, or readily substituted aromatic rings play a large part in determining the

<sup>&</sup>lt;sup>1</sup> Kleinberg, Chem. Revs., 40, 381 (1947).

<sup>&</sup>lt;sup>2</sup> Staněk, Chem. Listy, 47, 1244 (1953).

<sup>&</sup>lt;sup>2a</sup> Johnson and Ingham, Chem. Revs., 56, 219 (1956).

 $(\mathbf{E})$ 

course of the reactions. Thus, it is possible to produce (A) organic halides containing one less carbon atom than the original acid, RCO<sub>2</sub>H; (B) esters, RCO<sub>2</sub>R, derived from two molecules of the acid by loss of one molecule of carbon dioxide; (C) esters of 1,2-diols or of halohydrins; (D) halogenated aromatic compounds; and (E) halogenated acetylenes. These reactions may be represented by the following general equations.

(A) 
$$RCO_2Ag + X_2 \rightarrow RX + CO_2 + AgX$$

(B) 
$$2RCO_2Ag + X_2 \rightarrow RCO_2R + CO_2 + 2AgX$$

(AB) 
$$3RCO_2Ag + 2X_2 \rightarrow RCO_2R + RX + 2CO_2 + 3AgX$$

(C) 
$$RCO_2Ag + X_2 + R'CH = CHR'' \rightarrow R'CH(OCOR)CHXR'' + AgX$$
  $2RCO_2Ag + X_2 + R'CH = CHR'' \rightarrow R'CH(OCOR)CH(OCOR)R'' + 2AgX$ 

(D) 
$$\begin{split} \mathrm{RCO_2Ag} + \mathrm{X_2} + \mathrm{ArH} &\rightarrow \mathrm{RCO_2H} + \mathrm{ArX} + \mathrm{AgX} \\ \mathrm{ArCO_2Ag} + \mathrm{X_2} &\rightarrow \mathrm{X-Ar-CO_2H} + \mathrm{AgX} \\ \end{split}$$
 (E) 
$$\mathrm{RCO_2Ag} + \mathrm{X_2} + \mathrm{R'C} = \mathrm{CH} \rightarrow \mathrm{R'C} = \mathrm{CX} + \mathrm{RCO_2H} + \mathrm{AgX} \\ \end{split}$$

The reaction represented by A in which the molar silver salt-halogen ratio is 1:1, is due chiefly to Hunsdiecker;3-5 it makes available a variety of compounds that are prepared only with difficulty by other procedures. Reaction B is generally known as the Simonini reaction;6,7 it is carried out with a 2:1 molar ratio of silver salt to halogen (iodine only). Reaction AB, discovered by Oldham and Ubbelohde, makes use of a 3:2 molar ratio of reactants. Reactions C and E are usually attributed to Prévost. 9-14 Reaction D proceeds only in the presence of a phenyl group (Ar) which undergoes electrophilic substitution readily,15-18 or when R is of such a nature that the RCO<sub>2</sub> ion is a very weak base, such as CF<sub>3</sub>CO<sub>2</sub>. 19

- <sup>3</sup> Hunsdiecker, Hunsdiecker, and Vogt, U.S. pat. 2,176,181 (1939) [C. A., 34, 1685 (1940)].
- 4 Hunsdiecker and Hunsdiecker, Ber., 75, 291 (1942).
- <sup>5</sup> Hunsdiecker, Hunsdiecker, and Vogt, Ger. pat. 730,410 (1942) [C. A., 38, 374 (1944)].
- 6 Simonini, Monatsh., 13, 320 (1892).
- 7 Simonini, Monatsh., 14, 81 (1893).
- 8 Oldham and Ubbelohde, J. Chem. Soc., 1941, 368.
- 9 Prévost, Compt. rend., 196, 1129 (1933).
- 10 Prévost, Compt. rend., 197, 1661 (1933).
- 11 Prévost and Lutz, Compt. rend., 198, 2264 (1934).
- 12 Prévost, Compt. rend., 200, 942 (1935).
- 13 Prévost and Wiemann, Compt. rend., 204, 700 (1937).
- 14 Prévost and Wiemann, Compt. rend., 204, 989 (1937).
- 15 Birnbaum and Reinherz, Ber., 15, 456 (1882).
- 16 Barnes and Prochaska, J. Am. Chem. Soc., 72, 3188 (1950).
- 17 Dauben and Tilles, J. Am. Chem. Soc., 72, 3185 (1950).
- 18 Papa, Schwenk, and Klingsberg, J. Am. Chem. Soc., 72, 2623 (1950).
- 19 Haszeldine and Sharp, J. Chem. Soc., 1952, 993.

### NATURE OF THE REACTIONS

It is well established 20-22 that the primary product of the reaction between a dry silver salt of a carboxylic acid and halogen is an acyl hypohalite.

$$RCO_2Ag + N_2 + RCO_2X + AgX$$

Thermal cleavage of this intermediate results in the formation of an alkyl halide with loss of earbon dioxide, and this is the basis of reaction A.

$$RCO_2X \rightarrow RX + CO_2$$

Extensive evidence favors a mechanism with the free radical R as an intermediate in the conversion of RCO2Br to RBr. First the reaction of optically active silver salts with bromine or of the intermediate neyl hypobromites I and II under a variety of conditions leads to totally racemized bromides III and IV.23 Although the alkyl bromide, if it had

$$\begin{array}{cccc} {\rm C_2H_5CH(CH_3)CO_2Br} & & & n{\rm \cdot C_3H_7CH(C_2H_5)CO_2Br} \\ & & & {\rm II} & & \\ {\rm C_2H_5CH(CH_3)Br} & & n{\rm \cdot C_3H_7CH(C_2H_5)Br} \\ & & & {\rm II} & & \\ \end{array}$$

been obtained optically active in these reactions, would have been racemized slowly by the silver bromide present, it was shown by control experiments that such racemization is too slow to account for most of the loss of optical activity observed during the reaction of the silver salt with bromine. The reactions of optically active silver salts with bromine had previously been reported to yield optically inactive bromides,24-26 but the significance of the results remained in doubt since it was not shown at that time that the loss in activity was not entirely due to racemization of the bromide by silver bromide.

It should be mentioned that silver (+)-α-phenylpropionate was reported to react with bromine in earbon tetrachloride to yield phenothyl bromide with 43% of the optical activity retained.27 It has been shown, however, that (+)-phenethyl bromide, when boiled with silver bromide in carbon tetrachloride under conditions of the reaction of the silver salt with bromine, is essentially completely racemized.28,29 This would

<sup>&</sup>lt;sup>20</sup> Boekemüller and Hoffmann, Ann., 519, 165 (1935).

<sup>&</sup>lt;sup>21</sup> Birekenbach, Goubeau, and Berninger, Ber., 65, 1339 (1932).

<sup>&</sup>lt;sup>22</sup> Uschakov and Chistov, Bcr., 68, 824 (1935).

<sup>22</sup> Usehakov and Chistov, Ber., 00, 024 (Association).
23 Winstein and Berr, Unpublished work; C. E. Berr, Ph.D. Thesis, University of California, Los Angeles, 1952; Winstein, Bull soc. chim. France, [5] 18, 70a (1951).

<sup>&</sup>lt;sup>24</sup> Arnold and Morgan, J. Am. Chem. Soc., 70, 4248 (1948).

<sup>&</sup>lt;sup>25</sup> Heintzeler, Ann., 569, 102 (1950).

<sup>&</sup>lt;sup>26</sup> Bell and Smyth, J. Chem. Soc., 1949, 2372.

Bell and Smyth, J. Chem. Soc., 1949, 2010.
 Arcus, Campbell and Kenyon, Nature, 163, 287 (1949); J. Chem. Soc., 1949, 1510.

<sup>&</sup>lt;sup>28</sup> Abbott and Arcus, J. Chem. Soc., 1952, 3195.

<sup>&</sup>lt;sup>29</sup> Areus and Boyd, J. Chem. Soc., 1951, 1580.

indicate that the substance responsible for the optical activity observed in the product of the silver salt reaction was not phenethyl bromide. This conclusion has been strengthened by the failure of several investigators<sup>23</sup>, <sup>28</sup>, <sup>30</sup> to isolate any phenethyl bromide from the reaction of silver  $\alpha$ -phenylpropionate with bromine in earbon tetrachloride. A report<sup>28</sup> that silver (+)-2-ethylhexanoate with bromine gives (+)-3-bromoheptane requires further investigation.

That it is the intermediate  $R_1$ , rather than  $R^+$  or  $R^{-,31}$  which is responsible for the observed loss of activity during reaction has been supported by evidence from several sources. Thus, reactions that might have been expected to lead to the neopentyl carbonium ion invariably lead to products derived from its rearrangement product, the t-amyl carbonium ion.<sup>32</sup> Silver t-butylacetate, however, reacts with bromine to yield neopentyl bromide with no detectible amount of t-amyl bromide.<sup>23,33</sup> Similarly, reactions that might be expected to proceed by way of the cyclobutyl carbonium ion lead to mixtures of cyclobutyl, cyclopropyl-carbinyl, and allylearbinyl products.<sup>34</sup> The reaction of silver cyclobutanecarboxylate with bromine, however, yields cyclobutyl bromide accompanied by only a very small amount of rearranged products.<sup>35</sup>

While the neopentyl radical,  $(CH_3)_3CCH_2$ , does not rearrange under conditions used to prepare it, the neophyl radical,  $C_6H_5C(CH_3)_2CH_2$ , has been shown to rearrange in part to the more stable tertiary radical,  $(CH_3)_2CCH_2C_6H_5$ . Examination of the reaction of the acyl hypobromite V has indicated that some of the tertiary bromide VI was formed by

$$\begin{array}{ccc} \mathbf{C_6H_5C(CH_3)_2CH_2CO_2Br} & & \mathbf{BrC(CH_3)_2CH_2C_6H_5} \\ \mathbf{v} & & \mathbf{v_I} \end{array}$$

rearrangement in addition to the unrearranged product.<sup>23</sup> A control experiment showed that the unrearranged product, neophyl bromide, was stable toward the reaction conditions.

Additional evidence for the radical intermediate is provided by a study of the reaction of the silver salt of apocamphane-I-carboxylic acid.<sup>37</sup> Reactions proceeding by way of the apocamphyl carbonium ion have been

<sup>30</sup> Cason, Kalm, and Mills, J. Org. Chem., 18, 1670 (1953).

<sup>31</sup> Compare Rottenberg, Experientia, 7, 432, (1951) [C. A., 46, 4336 (1952)].

<sup>&</sup>lt;sup>32</sup> Ingold, Structure and Mechanism in Organic Chemistry, pp. 485–486, Cornell University Press, Ithaca, New York. 1953.

<sup>33</sup> Smith and Hull, J. Am. Chem. Soc., 72, 3309 (1950).

<sup>34</sup> Roberts and Mazur, J. Am. Chem. Soc., 73, 2509 (1951).

<sup>35</sup> Cason and Way, J. Org. Chem., 14, 32 (1949); Roberts and Chambers, J. Am. Chem. Soc., 73, 5039 (1951); Buchman and Conly, ibid., 75, 1990 (1953).

 <sup>36</sup> Urry and Kharasch, J. Am. Chem. Soc., 66, 1438 (1944); Winstein and Seubold, ibid.,
 69, 2916 (1947); Urry and Nicolaides, ibid., 74, 5162 (1952).

<sup>37</sup> Wilder and Winston, J. Am. Chem. Soc., 75, 5370 (1953).

shown to be very much slower than their counterparts in acyclic systems.<sup>38</sup> On the other hand, there is no such retardation when the apocamphyl radical is involved.<sup>39</sup> It was found, in fact, that silver apocamphane-1-carboxylate reacts readily with bromine in boiling petroleum ether to yield 1-bromoapocamphane in 50% yield, with no evidence of any retardation in rate by the bicyclic system. The reaction in carbon tetrachloride was accompanied by the formation of a chlorine-containing by-product.<sup>37</sup>

Other observations which are suggestive of a free-radieal chain mechanism are side-chain bromination of toluene, 19 the indication that there is an induction period when the reaction is carried out at low temperatures, 40 and an acceleration of the reaction by light. 20

The most probable mechanism would appear to be the following.41

Initiation 
$$RCO_2Br \rightarrow RCO_2 \cdot + Br \cdot$$
  
Propagation  $RCO_2 \cdot \rightarrow R \cdot + CO_2$   
 $R \cdot + RCO_2Br \rightarrow RBr + RCO_2 \cdot$   
Termination  $2R \cdot \rightarrow R - R$  or  $RH +$ olefin  $RCO_2 \cdot + R \cdot \rightarrow RCO_2R$ 

and/or

Another piece of evidence consistent with this picture is the following. The reaction of silver benzoate with bromine in carbon tetrachloride gives 53% of bromobenzene, 5% of chlorobenzene, and 6.7% of bromotrichloromethane. These products are readily explained if, superimposed on the sequence of reactions above, there is reaction of the phenyl radical with carbon tetrachloride as shown below. 16,17,\*

$$\begin{aligned} & \mathbf{C_6H_5^{\cdot}} + \mathbf{ClCCl_3} \rightarrow \mathbf{C_6H_5Cl} + \cdot \mathbf{CCl_3} \\ & \cdot \mathbf{CCl_3} + \mathbf{BrO_2CC_6H_5} \rightarrow \mathbf{BrCCl_3} + \cdot \mathbf{O_2CC_6H_5} \\ & \quad \text{(or BrBr)} \end{aligned}$$

<sup>38</sup> Bartlett and Knox, J. Am. Chem. Soc., 61, 3184 (1939).

<sup>39</sup> Kharasch, Engelmann, and Urry, J. Am. Chem. Soc., 65, 2428 (1943).

<sup>40</sup> Conly, J. Am. Chem. Soc., 75, 1148 (1953).

<sup>&</sup>lt;sup>41</sup> Compare Price, Mechanisms of Reactions at Carbon-Carbon Double Bonds, p. 55, Interscience Publishers, New York, 1946.

<sup>\*</sup>Wiberg and Shryne, 41a on the basis of the report that silver (+)-2-ethylhexanoatc with bromine gives (+)-3-bromoheptane, 28 suggested that the mechanism is a 1,3-intramolecular shift involving an electron-deficient group in the transition state—a mechanism first proposed by Rottenberg. 31 Since the reported rotention of optical activity in this reaction is in contradiction with the reports of racemization described on p. 335, caution must be exercised until confirmation is available.

<sup>&</sup>lt;sup>41a</sup> Wiberg and Shryne, J. Am. Chem. Soc., 77, 2774 (1955).

When the silver salt of a carboxylic acid reacts with iodine in a 2:1 molar ratio, the primarily formed acyl hypoiodite ecordinates with the excess silver salt to form a complex. 6,7,12-17a Many such complexes can be

$$\begin{split} & 2\mathrm{RCO_2Ag} + \mathrm{I_2} \rightarrow \mathrm{RCO_2I} + \mathrm{RCO_2Ag} + \mathrm{AgI} \\ & \mathrm{RCO_2Ag} + \mathrm{RCO_2I} \rightarrow \mathrm{RCO_2Ag} \cdot \mathrm{RCO_2I} \end{split}$$

isolated. With others, however, the difference between the temperatures of formation and decomposition is too small to permit isolation. thermal cleavage of the complex to give an ester is the basis of reaction B (Simonini reaction).

$$RCO_2Ag \cdot RCO_2I \rightarrow RCO_2R + CO_2 + AgI$$

It is not clear what role, if any, the complex formation plays in the reaction, which appears to be composed of two parts. Available evidence suggests that the first stage, a reaction of the silver salt with iodine to give earbon dioxide and alkyl iodide, is elosely related to the Hunsdieeker reaction discussed above. The second stage is an ionic reaction of the alkyl iodide thus formed with a second molecule of silver salt.19 This

$$\begin{split} \text{RCO}_2\text{Ag} + \text{I}_2 &\rightarrow \text{RCO}_2\text{I} + \text{AgI} \\ \text{RCO}_2\text{I} &\rightarrow \text{RI} + \text{CO}_2 \\ \text{RI} + \text{RCO}_2\text{Ag} &\rightarrow \text{RCO}_2\text{R} + \text{AgI} \end{split}$$

view is eonsistent with the fact that in the reaction of such substances as silver cyclobutaneearboxylate 44,48 a typical earbonium ion rearrangement occurs in the alcohol portion of the ester formed. The products are cyelobutyl, cyelopropylearbinyl, and allylcarbinyl eyelobutaneearboxylates in yields of 32, 65, and 3%, respectively.

$$\begin{array}{c} {\rm C_4H_7CO_2Ag + I_2 \rightarrow C_4H_7I + CO_2 + AgI} \\ {\rm C_4H_7I + AgO_2CC_4H_7 \rightarrow C_4H_7O_2CC_4H_7 + C_3H_5CH_2O_2CC_4H_7} \\ {\rm + CH_2 = CHCH_2CH_2O_3CC_4H_7} \end{array}$$

Failure to observe the formation of triplienylmcthyl peroxide when silver triphenylacetate is treated with iodine in the presence of air has been interpreted as evidence that the triphenylmethyl radical is not an intermediate.49 Such an argument is valid, however, only if it can be

- 42 Heiduschka and Ripper, Ber., 56, 1736 (1923).
- 43 Birnbaum and Gaier, Ber., 13, 1270 (1880).
- 44 Demjanov and Dojarenko, Ber., 40, 2594 (1907).
- 45 Gascard, Compt. rend., 153, 1484 (1911).
- 16 Gascard, Ann. chim. (Paris), [9] 15, 332 (1921).
- 47 Panies, Monatsh., 15, 10 (1894).
- 47a Birnbaum, Ann., 152, 111 (1869).
- 48 Roberts and Simons, J. Am. Chem. Soc., 73, 5487 (1951). 49 Wieland and Fischer, Ann., 446, 49 (1925-26).

shown that the reaction of the triphenylmethyl radical with oxygen under the conditions employed is faster than its reaction with iodine.

While the Hunsdiecker and Simonini reactions produce halides and esters respectively, the reaction represented by AB gives rise to both of these products. The iodine triacyl postulated as an intermediate can be isolated when R is a long-chain alkyl group. Formed by the action of 2 moles of iodine on 3 moles of the silver salt as indicated below, such compounds decompose thermally to yield both alkyl halide and ester.<sup>8</sup> In the

$$\begin{aligned} 3\mathrm{RCO_2Ag} + 2\mathrm{I_2} &\rightarrow \mathrm{I(OCOR)_3} + 3\mathrm{AgI} \\ \mathrm{I(OCOR)_3} &\rightarrow \mathrm{RCO_2R} + \mathrm{RI} + 2\mathrm{CO_2} \end{aligned}$$

presence of excess iodine, the iodine triacyl decomposes to give a high yield of alkyl iodide.

$$I(OCOR)_3 + I_2 \rightarrow 3RI + 3CO_2$$

Water decomposes the triacyl to yield iodine and iodic acid.

$$I(OCOR)_3 + 3H_2O \rightarrow I(OH)_3 + 3RCO_2H$$
  
 $5I(OH)_3 \rightarrow 3HIO_3 + I_2 + 6H_2O$ 

This, and the fact that triacyls such as iodine tris(trichloromethylacetate) conduct electricity with the iodine migrating toward the cathode, indicates the positive nature of the iodine in such materials.<sup>50</sup>

Nothing is known of the mechanism of these reactions. It seems likely, however, that they are radical chain reactions initiated by the dissociation of the iodine triacyl to acyl hypoiodite and acyloxy radicals. It is entirely reasonable that those acyloxy radicals that lose carbon dioxide

$$I(OCOR)_3 \rightarrow IOCOR + 2RCO_2$$

give alkyl radicals that react with iodine triacyl as shown below. A fuller

$$RCO_2 \rightarrow R \cdot \xrightarrow{I(OCOR)_3} RCO_2 R + IOCOR + RCO_2 \cdot$$

understanding of the mechanism must await further investigation.

In the presence of ethylenic compounds the primarily formed acyl hypohalite adds to the double bond to form a haloester.

$$RCO_2X + R'CH = CHR'' \rightarrow R'CH(OCOR)CHXR''$$

This is the basis of reaction C. The Simonini complex undergoes a similar reaction to yield first the ester of an iodohydrin and, finally, a diester. Presumably the complex dissociates, the acyl hypoiodite adds to the double bond, and the iodine is replaced by the molecule of silver salt formed by dissociation of the complex.<sup>10</sup>

$$\begin{aligned} & RCO_2I \cdot RCO_2Ag \rightarrow RCO_2I \ + RCO_2Ag \\ & RCO_2I \ + R'CH=CHR'' \rightarrow R'CH(OCOR)CHIR'' \\ & R'CH(OCOR)CHIR'' \ + RCO_2Ag \rightarrow R'CH(OCOR)CH(OCOR)R'' \ + AgI \end{aligned}$$

<sup>50</sup> Fichter and Stern, Helv. Chim. Acta, 11, 1256 (1928).

or

The products of the reaction suggest an ionic mechanism. Evidence that might be considered support for such a mechanism arises from the following fact: Silver (+) or (-)-2-ethylhexanoate when treated with bromine in carbon tetrachloride yields acyl hypohalites which add to styrene to give (+) or (-)-2-bromo-1-phenethyl-2-ethylhexanoate, which on hydrolysis with alkali yields (+) or (-)-2-ethylhexanoic acid in which a substantial percentage of the optical activity of the original acid is retained.<sup>51</sup> However, this reaction does not involve the asymmetric carbon atom and is not, therefore diagnostic as to mechanism. partial racemization presumably occurs during hydrolysis, for it has been shown that racemization of such esters can accompany hydrolysis.

Substitution of halogen in the benzene nucleus, as represented by reaction D, occurs most readily when R is the trifluoromethyl group. 19,52,53 However, if the aryl group is activated sufficiently to electrophilic attack, substitution may occur when R is methyl. The substituted products obtained are those expected through halogenation by an entity which carries a positive charge. Thus ortho and para substitution occur in compounds containing groups known to activate the aromatic nucleus to electrophilic attack, whereas substitution fails or occurs in the meta position when the substituent deactivates the nucleus. On this basis, the fission of the acyl hypohalite would be expected to proceed by an ionic mechanism. Thus, either the acyl hypohalite itself or X+ formed by its dissociation can serve as the halogenating agent.

$$\begin{split} \text{RCO}_2 \mathbf{X} + \mathbf{C}_6 \mathbf{H}_6 &\rightarrow \mathbf{C}_6 \mathbf{H}_5 \mathbf{X} + \mathbf{H}^+ + \mathbf{RCO}_2^- \\ \\ \text{RCO}_2 \mathbf{X} &\rightarrow \mathbf{RCO}_2^- + \mathbf{X}^+ \\ \mathbf{X}^+ + \mathbf{C}_6 \mathbf{H}_6 &\rightarrow \mathbf{C}_6 \mathbf{H}_5 \mathbf{X} + \mathbf{H}^+ \end{split}$$

Fission by a free-radical mechanism would necessitate halogenation by halogen atoms. When an alkyl side chain is present, substitution of the side chain is the preferred reaction. However, the products of such a process have not been found in any of the reactions studied.

When the acyl hypohalite is derived from an ordinary alkyl or aryl carboxylic acid, it is a sufficiently poor halogenating agent in the absence of readily substituted aromatic rings to allow the free-radical dissociation followed by decarboxylation (Hunsdiecker reaction) to predominate. However, nuclear halogenation can be increased at the expense of the Hunsdiecker reaction either by adding a readily substituted aromatic compound such as veratrole<sup>53a</sup> or by using a more active acyl hypohalite

<sup>51</sup> Abbott and Arcus, J. Chem. Soc., 1952, 1515.

<sup>52</sup> Henne and Zimmer, J. Am. Chem. Soc., 73, 1362 (1951).

<sup>53</sup> Schwartz, Anales soc. españ. fis. quim., 27, 683 (1929) [C. A., 24, 589 (1930)]. 534 Janssen, Van Allan, and Wilson, J. Org. Chem., 20, 1326 (1955).

as the halogenating agent. Trifluoroacetyl hypobromite shows little tendency to undergo the Hunsdiecker decarboxylation at temperatures ordinarily employed with other acyl hypohalites. It is, therefore, particularly useful as a brominating agent.<sup>19,52</sup>

The other phase of reaction D involves the presence of readily substituted aromatic rings in the silver salt and thus in the acyl hypohalite. Again, either the hypohalite itself or X<sup>+</sup> formed by its dissociation acts as the halogenating agent.<sup>17</sup>

Substitution of halogen in acetylenes, as indicated by reaction E, probably occurs by a similar mechanism.

or 
$$RCO_{2}X + R'C = CH \rightarrow R'C = CX + H^{+} + RCO_{2}^{-}$$
$$RCO_{2}X \rightarrow RCO_{2}^{-} + X^{+}$$
$$X^{+} + R'C = CH \rightarrow R'C = CX + H^{+}$$

#### SCOPE AND LIMITATIONS OF THE REACTIONS

## Thermal Cleavage of Acyl Hypohalites (Hunsdiecker Reaction)

The thermal decomposition of acyl hypohalites formed as intermediates in the halogen silver-salt reaction to produce compounds containing one carbon atom less than the original acid is perhaps the most important of the various silver salt-halogen reactions. The reaction is of general application in the aliphatic series, leading, with simple fatty acids of 2 to 18 carbon atoms, to excellent yields of alkyl halides.<sup>3,20,25,30,54-58</sup>

$$\mathrm{RCO_2Ag} + \mathrm{X_2} \rightarrow \mathrm{RX} + \mathrm{CO_2} + \mathrm{AgX}$$

A substituent in the aliphatic chain in any position other than the

<sup>&</sup>lt;sup>54</sup> Lüttringhaus and Schade, Ber., 74, 1565 (1941).

Mehta, Mehta, and Thosar, J. Indian Chem. Soc., Ind. Ed., 3, 137 (1940).

<sup>56</sup> Borodine, Ann., 119, 121 (1861).

<sup>&</sup>lt;sup>57</sup> Birnbaum, Ann., 152, 111 (1869).

<sup>58</sup> Cason and Winans, J. Org. Chem., 15, 142 (1950).

α-position does not interfere with the reaction unless it is itself eapable of reaction with the aeyl hypohalite. Thus, silver salts of alkyl-substituted fatty acids yield primary halides as do acids carrying a cycloalkyl substituent such as cyclopentylacctic acid.<sup>5</sup> Simple halogen derivatives, such as silver β-bromopropionate, yield dibromides. 40 Polyhalogen compounds have been obtained from silver salts of polyhalogen aeids; thus, silver 9,10-dichloroöctadecanoate yields 1-bromo-8,9-dichloroheptadeeanc;3 and 1,8,9,11,12-pentabromoheptadecane is obtained from silver 9,10,12,13tetrabromoöctadecanoate. 59 When applied to acid esters, the reaction leads to ω-halo esters. 4,5,60-62 This is a useful reaction because ω-halo

$$RO_2C(CH_2)_nCO_2Ag + X_2 \rightarrow RO_2C(CH_2)_nX + CO_2 + AgX$$

esters are not easily prepared by other procedures. Silver salts of acids in which there is an aryl substituent such as phenyl25,63 or deactivated phenyl<sup>16</sup> also give primary halides. If, however, the substituent is a phenyl group readily substituted by electrophilie agents, there is halogenation of the ring and formation of a free acid without loss of earbon dioxide. For example, silver  $\beta$ -3-methoxyphenylpropionate when treated with bromine or iodine gives an excellent yield of  $\beta$ -2-bromo-(or iodo-)5methoxyphenylpropionie aeid. 18 Such complex substances as  $3(\alpha)$ ,  $12(\beta)$ diacetoxynordesoxyeholanic acid (VII) and  $\hat{3}$  ( $\alpha$ ), 12( $\beta$ )-diacetoxyeholanie

$$\text{CH}_2\text{CH}_2\text{CO}_2\text{Ag} + \text{Br}_2 \rightarrow \text{CH}_3\text{C} \rightarrow \text{CH}_2\text{CH}_2\text{CO}_2\text{H} + \text{AgX}$$

$$\begin{array}{c|c} \operatorname{CH_3CO_2} & \operatorname{CH_3} & \operatorname{CH_3} \\ \operatorname{CH_3CO_2} & \operatorname{CH_3} & \operatorname{CH_2CH_2CO_2H} \\ \\ \operatorname{CH_3CO_2} & \operatorname{CH_3} & \operatorname{CH_3} \\ \\ \operatorname{CH_3CO_2} & \operatorname{CH_3} & \operatorname{CHCH_2CO_2H} \\ \end{array}$$

VIII

or the wa

<sup>59</sup> Howton, Davis and Nevenzel, J. Am. Chem. Soc., 74, 1109 (1952).

<sup>60</sup> Allen and Wilson, Org. Syntheses, 26, 52 (1946).

<sup>61</sup> Duschinsky and Rubin, J. Am. Chem. Soc., 70, 2546 (1948). 62 Stoll and Rouve, Helv. Chim. Acta, 34, 98 (1951).

<sup>63</sup> Oldham, J. Chem. Soc., 1950, 100.

silver bromide, for 2-bromobieyclo[2.2.2]octane and silver bromide give the same product. By operating at -10°, it has been possible to isolate the expected bromide as well as the rearranged product.<sup>69</sup>

$$\begin{array}{c|c} & & & & \\ \hline \begin{array}{c} CH_2 \\ CH_2 \end{array} \\ \hline \begin{array}{c} CO_2Ag \\ \hline \\ CH_2 \end{array} \\ \hline \begin{array}{c} CCI_4 \\ \hline \\ CH_2 \end{array} \\ \hline \end{array} \begin{array}{c} CH_2 \\ \hline \\ CH_2 \end{array} \\ \hline \begin{array}{c} Ag \ Br \\ \hline \\ CH_2 \end{array} \\ \hline \end{array} \begin{array}{c} CH_2 \\ \hline \end{array} \begin{array}{c} Br \\ \hline \end{array}$$

Silver salts of simple carboxylie acids having a tertiary  $\alpha$ -carbon atom, such as silver trimethyl- and triphenyl-acetate, yield a variety of products when treated with bromine.<sup>25</sup> However, the silver salts of the complex alicyclie acids, adamantanedicarboxylie acid (IX)<sup>70</sup> and bicyclo[3.3.1]-nonan-9-one-1-carboxylic acid (X)<sup>71</sup> give the corresponding bromides in yields of 28 and 74%, respectively. These acids cannot be decarboxylated directly; the silver salt-halogen reaction, therefore, serves as an intermediate step in the preparation of the parent hydrocarbons.

The reaction has been used successfully as a preliminary step in the synthesis of cantharadin from the silver salt (XI) of the 2,3-dimethyl ester of 2,3-dimethyleyelohexane-1,2,3,4-tetracarboxylic acid. Treatment of this silver salt with bromine in earbon tetrachloride results in a lactone XII, formed by loss of methyl bromide from the primarily formed dibromide. Saponification and pyrolysis of the lactone gives a mixture of cantharic acid (XIII) and cantharadin (XIV). (Formulas on p. 345.)

When substituents other than alkyl or aryl are present in the  $\alpha$ -position, the decarboxylation leads to a variety of products. The silver salts of  $\alpha$ -halogen acids yield 1,1-dihalogenated hydrocarbons. Many di-, tri-, and tetra-halogenated methanes, exemplified by such substances as

$$RCHXCO_2Ag + X'_2 \rightarrow RCHXX' + CO_2 + AgX'$$

CH\_CIF, CHBrCIF, CBr<sub>2</sub>F<sub>2</sub> have been prepared by this reaction.<sup>73</sup> Any combination of hydrogen and halogen may be present in the silver salt,

$$RRR^*CCO_2Ag + X_2 \rightarrow RR^*R^*CX + CO_2 + AgX$$

$$\begin{array}{c} AgO_2C \\ CH_3 \\ CO_2CH_3 \\ CO_2CH_3 \\ CH_3 \\$$

and X may be ehlorine, bromine, or iodine. The yields vary widely (see Table V). Perfluoro aeids give perfluoroalkyl halides. 73-80

$$\mathrm{CF_3(CF_2)_nCO_2Ag} \ + \ \mathrm{X_2} \rightarrow \mathrm{CF_3(CF_2)_nX} \ + \ \mathrm{CO_2} \ + \ \mathrm{AgX}$$

temperature is required because of the stability, mentioned earlier, of the trifluoroaeetoxy radical toward decarboxylation. This is probably true to a smaller extent with the silver salts of various halogenated derivatives of acetic acid.

Other a-substituted acids that undergo the reaction include a-keto, α-hydroxy, and α-amino acids; α-keto acids give acyl halides whereas the hydroxy and amino acids lead to aldehydes. If the remaining hydrogen atom on the  $\alpha$ -earbon atom of the hydroxy and amino acids is replaced by

$$\begin{aligned} & \operatorname{RCOCO_2Ag} + \operatorname{X_2} \rightarrow \operatorname{RCOX} + \operatorname{CO_2} + \operatorname{AgX} \\ & \operatorname{RCHOHCO_2Ag} + \operatorname{X_2} \rightarrow \operatorname{RCHO} + \operatorname{CO_2} + \operatorname{AgX} + \operatorname{HX} \\ & \operatorname{RCHNH_2CO_2Ag} + \operatorname{X_2} \rightarrow \operatorname{RCHNH_2X} + \operatorname{CO_2} + \operatorname{AgX} \\ & & \underbrace{ \operatorname{H_2O}} \operatorname{RCHO} + \operatorname{NH_4X} \end{aligned}$$

an alkyl group, ketones result. For the most part, these reactions are considered only in the original patent,3 and little work has been done on their development. Heyns and Stange, however, have shown that the

<sup>74</sup> Hauptschein and Grosse, J. Am. Chem. Soc., 73, 2461 (1951).

<sup>75</sup> Hauptschein, Kinsman, and Grosse, J. Am. Chem. Soc., 74, 849 (1952).

<sup>76</sup> Brice and Simons, J. Am. Chem. Soc., 73, 4016 (1951).

<sup>77</sup> Henne and Finnegan, J. Am. Chem. Soc., 72, 3806 (1950).

<sup>78</sup> Haszeldine, J. Chem. Soc., 1951, 584.

<sup>79</sup> Hauptschein, Nodiff, and Grosse, J. Am. Chem. Soc., 74, 1347 (1952).

<sup>80</sup> Henne and Francis, J. Am. Chem. Soc., 75, 993 (1953).

silver salts of acylated  $\alpha$ -amino acids give halogen derivatives that can be isolated.<sup>81</sup> On hydrolysis these products form the carbonyl derivative, amide, and hydrogen halide.

$$\begin{split} & \text{RCHNH(COR')CO}_2\text{Ag} + \text{X}_2 \rightarrow \text{RCHBr(NHCOR')} + \text{CO}_2 + \text{AgX} \\ & \text{RCHBr(NHCOR')} + \text{H}_2\text{O} \rightarrow \text{RCHO} + \text{R'CONH}_2 + \text{HBr} \end{split}$$

The silver salt of ethylmalonie acid, which may be considered an  $\alpha$ -carboxy acid, gives a small yield of 1,1-dibromopropane together with some 1,1,1-tribromopropane; the tribromo derivative is presumably the result of some bromination before decarboxylation.<sup>40</sup> The potassium salts of the closely related alkyl  $\alpha$ -carbethoxyacetic acids yield  $\alpha$ -bromo<sup>82</sup> and  $\alpha$ -chloro<sup>53</sup> fatty acid esters. Again there is some halogenation before

$${\rm R'O_2CCHRCO_2K} + {\rm X_2} \rightarrow {\rm R'O_2CHXR} + {\rm CO_2} + {\rm KX}$$

decarboxylation. The best yields result from compounds of intermediate chain length (6-8 carbon atoms).

The silver salts of unsaturated acids have not been useful in this reaction. Silver methacrylate added to bromine in earbon tetrachloride at 0° gives a polymeric product. Silver allylacetate yields a bromolactone. 40 Because of the ease with which acyl hypohalites add to the olefinic bond (see p. 350), a clear-cut reaction would not be expected. However, silver phenylpropiolate and iodine produce phenyliodoacetylene in excellent yield. 12

Treatment of silver salts of α,ω-dicarboxylic acids with halogen leads to α, ω-dihalides,³,²₀,⁴₀,⁵ҳ,ҫ₃,ѕҳ Although this reaction is general, the yields of dihalide are poor with the lower members of the series. The formation of a broino compound from silver succinate and bromine was observed by Bunge as early as 1870,⁵⁵ However, the yield is small even when the silver salt is added to a solution of bromine in earbon tetrachloride,¹⁰ Silver glutarate and various alkyl-substituted derivatives give mainly γ-lactones though a small amount of dihalide is formed.⁵⁵

$$\Lambda_{\mathcal{G}} O_2 CCR_2 CR_2 CR_2 CO_2 \Lambda_{\mathcal{G}} + X_2 \rightarrow \underbrace{CR_2 CR_2 CR_2 CO_2}_{} + CO_2 + 2 AgX$$

are obtained.<sup>86</sup> With silver adipate there is some lactone formation, but a substantial yield of dibromide is obtained by the reverse addition procedure.<sup>84</sup> The higher members of the series give moderately good yields of dihalides. In the one instance in which a tricarboxy acid was used, the yield of trihalide was very small.<sup>40</sup>

Effect of the Halogen Employed. Bromine is most generally used in the Hunsdiecker reaction. In the few instances in which chlorine has been employed the yields have been satisfactory. 3,52,73,75,83,87 Iodine was normally used in a 1:2 molar ratio with the silver salts in the early work, and, consequently, the so-called Simonini ester was the main product. More recent work 87 has shown that an iodine-to-silver ratio of 1:1 affords substantial yields of the iodide, though some ester is produced. In fact, the yield of iodide rises, and that of the ester falls as the ratio of iodine to silver is gradually increased from 1:2 to 1:1. In the presence of excess iodine, the silver salts of the long-chain acids give good yields of the iodides. 8 Excellent yields of iodides have also been obtained from the silver salts of fluoro and perfluoro acids, 73 but the use of iodine in the preparation of iodides by this reaction has not been investigated thoroughly. It may well serve as a method for producing alkyl iodides as well as bromides.

Effect of Temperature. The effect of temperature has not been studied systematically. From available reports, it appears that the optimum temperature depends upon the silver salt used. Bromobenzene, for example, is obtained in 80% yield when bromine is added to a suspension of silver benzoate in boiling carbon tetrachloride,20 but the yield is insignificant when the reaction is carried out in the cold.20,54 Mehta and co-workers point out that carbon tetrachloride is a better solvent than chloroform for the reaction and indicate that its higher boiling point is responsible for the advantage.87 They show that better yields of longchain alkyl halides are obtained in boiling than in cold carbon tetrachloride. On the other hand, cyclobutyl bromide is obtained only when the reaction is run in carbon tetrachloride below  $-20^{\circ}.35$  In some instances, operation at a low temperature is necessary because of the instability of the silver The silver salts of  $\alpha$ -bromovaleric acid,  $\beta$ -bromopropionic acid. α-bromobutyric acid, and δ-bromovaleric acid, for example, are stable at  $0^{\circ}$  but not at room temperature. Silver  $\beta$ -bromopropionate changes into eta-propiolactone on drying in a desiccator at room temperature. 40 Nevertheless, these silver salts undergo the Hunsdiecker reaction at 0° to give fairly good yields of the corresponding bromides.

Effect of Solvent. Carbon tetrachloride is probably the best general

<sup>86</sup> Hauptschein, Stokes, and Grosse, J. Am. Chem. Soc., 74, 848 (1952).

<sup>87</sup> Mehta, Mehta, and Thosar, J. Indian Chem. Soc., Ind. Ed., 3, 166 (1940).

solvent for the reaction, although there are isolated instances in which other solvents produce better results. The production of n-propyl bromide from silver butyrate, for example, is carried out in nitrobenzene; if carbon tetrachloride is used, separation of the n-propyl bromide from the solvent is difficult because the two materials have approximately the same boiling point.20 Experiments carried out by Oldham and Ubbelohde have shown that good yields of undecyl iodide can be obtained in benzene (72-80%), carbon tetrachloride (70-78%), or petroleum ether (51-65%). In the few instances recorded in which the silver salt was used in carbon  ${\it disulfide, the yields\ were\ low.} {\it ^{25}\, Though\ Cason\ and\ Way\ prepared\ eyclobutyloop}$ bromide by operating in carbon tetrachloride at a low temperature,35 the same halide has also been made by treatment of the mercurie salt of the acid with bromine in carbon disulfide. 5 Dichlorodifluoromethane has been used successfully as a solvent in the preparation of eyclopropyl bromide67 and ethyl 4-bromobicyelo[2.2.2]octane-1-carboxylate.88 Tetrachloroethane was also used as a solvent in the former reaction, but the yield was poor. Chloroform, 3,8 ether, 3,89 ethyl bromide, 65,65a and trichloroethylene62 have also been used. In trichloroethylene a surprisingly good yield of methyl w-bromopentadecanoate was obtained from the requisite acid ester. Treatment of the silver salts of perfluoro acids with halogens is usually carried out without a solvent, 52,73-75,77,78 but in one instance perfluorotributylamine has been used successfully.76

Salts of Other Metals. Though silver salts have been generally used in this reaction, other salts have also been employed with varying success. Of these, the mercurous and mercuric salts have given the best results.3-5 Thallium salts have also been satisfactory.3 With some substituted malonic acid half-esters, the potassium salts have been used with yields varying from 23 to 80%. 82,83 The yields are highest when the substituent is n-butyl, n-hexyl, benzyl, or cyclohexyl and drop off rapidly when the number of carbons in the substituent is increased or decreased. Trifluoroacetic acid gives poorer yields of trifluoromethyl iodide when the sorlium, potassium, barium, mercury, or lead salt is employed in place of the silver salt. The reaction is carried out in a steel autoclave at a high temperature,78

Since esters are usually secured more easily by other procedures, the reaction has little value as a synthetic method. It has been of primary interest in connection with the mechanism of formation and decomposition of the complex, and because of a useful synthesis in which the complex is used, viz., the Prévost reaction (see p. 350).

Those silver salts that undergo the Hunsdiecker reaction readily also, in general, undergo the Simonini reaction. Only in the case of silver salts of saturated monocarboxylic acids is any difference discernible. The difference appears to be due to an ability of the primarily formed hypoiodites to give complexes or coordination compounds with the silver salt, an ability that apparently is not shared to any great degree by the acyl

$$\mathrm{RCO_2Ag} + \mathrm{RCO_2I} \rightarrow \mathrm{RCO_2Ag} \cdot \mathrm{RCO_2I}$$

hypobromites though a small quantity of ester is formed occasionally. Acyl hypoiodites also form stable coordination complexes with tertiary bases such as pyridine and  $\alpha$ -picoline.<sup>90</sup>

In the dibasic acid series, the products obtained by the Simonini procedure are comparable to those obtained with bromine. Silver oxalate yields only carbon dioxide and silver halide. Silver malonate produces carbon dioxide, but no other product has been identified. Silver succinate regenerates succinic acid and forms a little maleic anhydride, while silver glutarate and various substituted derivatives give  $\gamma$ -lactones in fair yields (40%). The method has been suggested as a preparative procedure for  $\gamma$ -lactones. Similar products are obtained with bromine. Silver adipate yields a small amount of polymerized  $\delta$ -valerolactone. The reaction with homologs higher than adipic acid has not been investigated.

Unsaturated acids do not give clear-cut results. Although the intermediate complex is formed in many cases and carbon dioxide is lost in the decomposition, the only other products identified are the unchanged acid or its anhydride. 43,49 Hydroxy acids yield aldehydes or ketoncs. This reaction, first reported by Herzog and Leiser, 89 proceeds as well with bromine as with iodine. Thus, formaldehyde is formed from glycolic acid, while mandelic acid yields benzaldehyde.

In the aromatic scries, the reaction has no value. Silver benzoate gives a variety of products including ester, halide, and halogenated benzoic acid.<sup>49</sup> Silver phthalate leads to phthalic anhydride, whereas silver hexahydrophthalate gives no identifiable products.<sup>49</sup>

<sup>&</sup>lt;sup>20</sup> Zingaro, Goodrich, Kleinberg, and VanderWerf, J. Am. Chem. Soc., 71, 575 (1949).

<sup>&</sup>lt;sup>21</sup> Windaus and Klänhardt, Ber., 54, 581 (1921).

<sup>&</sup>lt;sup>92</sup> Windaus, Klänhardt, and Reverey, Ber., 55, 3981 (1922).

<sup>&</sup>lt;sup>93</sup> Goldschmidt and Gräfinger, Ber., 68, 279 (1935).

#### Thermal Cleavage of Iodine Triacyls

A reaction somewhat similar to the Simonini reaction takes place when a silver salt and iodine react in a 3:2 molar ratio.8 The product contains positive, trivalent iodine but no silver. It is presumably an iodine triacyl, which decomposes thermally to produce both ester and alkyl

$$I(OCOR)_3 \xrightarrow{Heat} RCO_2R + RI + 2CO_2$$

halide. Heating in the presence of excess iodine gives the alkyl iodide only.

$$I(OCOR)_3 + I_2 \rightarrow 3RI + 3CO_2$$

#### Addition Reactions of Acyl Hypohalites (Prévost Reaction)

The intermediates formed in the Simonini and Hunsdiecker reactions, RCO2Ag·RCO2I and RCO2X, respectively, will react with olefins, acetylenes, and sufficiently reactive phenyl groups. The addition to olefins was first reported by Birekenbaeh, Goubeau, and Berninger,21 who treated silver acetate with iodine in ether solution, removed the silver iodide formed, and treated the filtrate with eyelohexene. The acctate of 2-iodocyclohexanol resulted. The same substance had been obtained by Brunel some years earlier in a similar reaction with mercuric acctate,

$$\begin{array}{c} \text{('II}_3\text{('O}_2\Lambda g \,+\, I_2 \,+\, \bigcirc ) \xrightarrow{\text{(C}_2\text{II}_3)_2\text{O}} \\ \end{array} \\ \begin{array}{c} \text{(CCOCH}_3 + \text{AgI} \\ \end{array}$$

iccline and cyclohexene.94 However, the method has been developed mainly by Prévost, 9-11,13,14 and the reaction is generally known by his name. Its chief use lies in the preparation of 1,2-glyeols.

When the Simonini complex obtained from silver benzoate and iodine is treated in benzene solution with an olefin, silver iodide precipitates and the dibenzoate of a 1,2-glycol is formed. Although the complex from 

Although benzoates are recommended, silver salts of acetic, 10,22 propionic,22 and butyric acids20,22 have also been used, especially in the preparation of the halo esters. Indeed, the second phase of the reaction of an olefin with silver acetate and an equimolar amount of iodine in benzene solution is slow, and the diester is accompanied by iodo acetates which are difficult to remove.10

The reaction also proceeds with silver salts of dicarboxylic acids. Thus, silver succinate, iodine, and cyclohexene in ether solution give di-2-iodocyclohexyl succinate. A small quantity of polymeric diester

$$\begin{array}{l} \mathrm{CH_2CO_2Ag} \\ | \\ \mathrm{CH_2CO_2Ag} \\ \end{array} + \mathrm{I_2} + 2 \end{array} \\ \rightarrow \begin{array}{l} \mathrm{CH_2CO_2C_6H_{10}I}\text{-}o \\ | \\ \mathrm{CH_2CO_2C_6H_{10}I}\text{-}o \\ \end{array} + 2\mathrm{AgI} \\ \end{array}$$

 $(C_{10}H_{14}O_4)_n$  is formed simultaneously. Silver salts of oxalic and phthalic acids and even silver carbonate undergo similar reactions.95

Silver 3,5-dinitrobenzoate has been suggested as a reagent for identification of olefins. Simple olefins like ethylene and propylene give the 3,5-dinitrobenzoate of the iodohydrin when treated with equimolar amounts of iodine and silver 3,5-dinitrobenzoate.96 When unsymmetrical

$$3.5 \cdot (NO_2)_2 C_6 H_3 CO_2 Ag + I_2 + RCH = CHR' \rightarrow$$

$$RCHICH[OCOC_6H_3(NO_2)_2]R' + AgI$$

olefins are used, the halogen appears exclusively on the less highly substituted carbon atom. This mode of addition, however, is not general, for preformed hypohalites from acetic, butyrie, and benzoic acids add to allyl halides to give good yields of 2,3-dihalogenated propyl esters.20,97

Bromine or ehlorine can be used in place of iodine.14,22,51 With these halogens, however, it is advantageous to earry out the reaction in earbon tetraehloride rather than benzene, to avoid the undesirable side reaction with the latter solvent which leads to the formation of phenyl benzoate.14 In the absence of detail in Prévost's papers, one is inclined to favor earbon tetraehloride as a solvent for all of the halogens. However, benzene has been used successfully by other experimenters.98,99

Studies on the addition of the complex from silver benzoate and iodine to butadiene have shown that the primary addition is mainly 1:2. Fractionation of the glycols obtained from the action of a limited quantity of the complex with butadienc gave 80% 1,2-glycol and 4% 1,4-glycol.11

The reaction has been applied to the mixture of monohydric phenols

<sup>95</sup> Birekenbach, Goubeau, and Kolb, Ber., 67, 1720 (1934).

<sup>&</sup>lt;sup>96</sup> Halperin, Donahoe, Kleinberg, and VanderWerf, J. Org. Chem., 17, 623 (1952).

<sup>97</sup> Edwards and Hodges, J. Chem. Soc., 1954, 761.

<sup>18</sup> Hershberg, Helv. Chim. Acta., 17, 351 (1934).

<sup>39</sup> Niemann and Wagner, J. Org. Chem., 7, 227 (1942).

on the silver salts of the unhalogenated acids. Silver  $\beta$ -(p-nitrophenyl)-propionate, however, gives p-nitrophenethyl bromide in excellent yield. 16

Although the method has little practical value for reasons that will appear below, it has been used to prepare a series of halogenated alkoxyphenyl fatty acids of the general formula.<sup>18</sup>

$$\overset{\text{RO}}{\overbrace{\widetilde{X}}} (\text{CH}_2)_n \text{CO}_2 \text{H}$$

The preparation of the silver salt of the acid to be halogenated is unnecessary. It is sufficient to use dry silver acetate in combination with the halogen; the acyl hypohalite first formed is the active halogenating agent.<sup>17,18</sup> The reaction is carried out in acetic acid or carbon tetrachloride. It proceeds as indicated only when a phenyl group active

$$(CH_2)_nCO_2H + CH_3CO_2Ag + X_2 \rightarrow X$$

$$(CH_2)_nCO_2H + AgX + CH_3CO_2H$$

$$RO$$

toward electrophilic substitution is present. It is, therefore, quite limited in application. The method is preferred to the mercuric acetate-iodine procedure because of the difficulty of removing mercuric iodide from organic solvents in which it is soluble; silver iodide can be removed quantitatively by filtration.

The silver salts of a variety of carboxylic acids react with iodine in the presence of benzenc to yield, among other products, iodobenzene and/or the phenyl ester of the carboxylic acid. The yield of iodobenzene is highest from silver o-nitrobenzoate. In the absence of benzene, however, this silver salt on treatment with bromine gives a 95% yield of o-nitrobromobenzene—the Hunsdiecker product. Benzene, therefore, is not a good solvent for reactions involving acyl hypohalites because it enters into competition for the halogen. When the acyl hypohalite undergoes the Hunsdiecker reaction sufficiently rapidly, benzene can be used as a solvent. This is the case when R is a long chain such as n- $C_{11}H_{23}$  or n- $C_{17}H_{35}$ .

The reaction between silver trifluoroacetate and iodine to yield carbon dioxide, silver iodide, and trifluoromethyl iodide does not occur appreciably

<sup>103</sup> Birckenbach and Meisenheimer, Ber., 69, 723 (1936).

below 100°,77 and silver trifluoroacetate-halogen is, therefore, a useful halogenating agent. Excellent yields of bromo- and iodo-benzenes eontaining methyl, halogen, methoxyl, amino, dimethylamino, and carboxyl groups as substituents are obtained by this procedure. <sup>19,52</sup> Benzene is so deactivated, however, by the introduction of a nitro group that the normal Hunsdiecker product, CF<sub>3</sub>I, is produced in 75% yield when nitrobenzene is treated with silver trifluoroacetate and iodine.

Normally no solvent is used in these reactions though earbon tetrachloride has been used successfully.<sup>52</sup> Nitrobenzene is often a suitable solvent.

The halogen enters in the para position to the group already present in the benzene derivative if the latter normally directs to that position. Infrared analyses indicate that a small amount of the ortho isomer is usually present. Benzoic acid is halogenated in the meta position, and there is no indication of ortho or para halogenation.

Although silver trifluoroacetate-halogen is not so powerful a halogenating agent as silver perchlorate-halogen, it possesses certain specific advantages.<sup>19</sup> Trifluoroacetic acid, formed in the reaction, is volatile and is easily removed by distillation. The danger attending the use of silver perchlorate is avoided. Silver trifluoroacetate is more soluble in organic solvents than silver trichloroacetate, acetate, perchlorate, or sulfate.<sup>19</sup>

It has been demonstrated that the Simonini complex from silver benzoate reacts with acetylenes to give excellent yields of iodoacetylenes. With phenylacetylene, the formation of phenyliodoacetylene is quantitative and benzoic acid and silver benzoate have been isolated in quantities corresponding to the following equation. <sup>12</sup> Acetylene itself reacts with

$$\begin{split} & \quad C_6 H_5 CO_2 Ag \cdot C_6 H_5 CO_2 I + C_6 H_5 C = CH \\ & \quad + C_6 H_5 C = CI + C_6 H_5 CO_2 H \\ & \quad + C_6 H_5 CO_2 Ag \end{split}$$

either one or two molecules of the complex to give iodo- and diiodo-acetylene, respectively. 12

It is not necessary to isolate the complex; addition of the acetylene derivative to the complex formed in benzene is satisfactory. However, the use of benzene as a diluent is not practical with chlorine or bromine because it takes part in the reaction. Carbon tetrachloride is satisfactory. Thus, the treatment of silver benzoate in carbon tetrachloride with bromine, chlorine, or iodine followed by addition of 1-heptyne gives good yields of the respective haloacetylenes.<sup>14</sup>

Prévost assumes that the Simonini complex is formed with chlorine and bromine in the same manner as with iodine. Such a complex has not been isolated with these halogens, nor is it necessary to assume that it

forms. The reaction could proceed equally well with the intermediate acyl hypohalite.

 $RCO_2X + R'C \equiv CH \rightarrow R'C \equiv CX + RCO_2H$ 

# EXPERIMENTAL PROCEDURES Preparation of Silver Salts

Two general methods are available for preparing the silver salts. The simplest and most direct method is the reaction between the potassium or sodium salt of the acid and silver nitrate. For acids of low molecular weight and for most dibasic acids, this is the most satisfactory method. For the higher acids (above C<sub>8</sub>) especially when fairly large quantities are employed, it has been suggested that freshly prepared silver oxide be used. Reaction of the potassium or sodium salts of the higher acids with silver nitrate leads to voluminous precipitates which are difficult to filter. For acids that are sparingly soluble in water the use of ethanolwater mixtures is recommended. For perfluoro acids unstable in water

(undecafluorocyclohexanecarboxylic acid, for example), the use of silver oxide is a necessity. With these acids the reaction is run in perfluorobutyl ether as a solvent. A representative preparation by each of these methods

It is essential to the success of the subsequent reactions with

the halogens to have the silver salts perfectly dry.

Silver Laurate.<sup>54</sup> Hot solutions of 50 g. of silver nitrate in 100 ml. of water and 59 g. of lauric acid in 200 ml. of 1.45 N potassium hydroxide are added simultaneously to 100 ml. of hot water with stirring. The addition is controlled so that approximately equivalent quantities of the reactants are present at all times. The precipitated silver salt is collected on a filter, washed with water and acetone, and air-dried. This material is powdered and then dried in a vacuum at 60° over phosphorus pentoxide.

The yield is 85 g. (94%).

Silver Methyl Octadecanedioate.<sup>4</sup> The silver oxide precipitated by the admixture of water solutions of 270 g. of silver nitrate and 150 g. of potassium hydroxide is washed free from alkali. The moist oxide is added to 520 g. of molten methyl hydrogen oetadecanedioate and stirred vigorously while boiling water is added. The silver salt formed is eolleeted on a filter, washed with hot ethanol, dried, finely powdered, and redried. The yield is 637 g. (99%).

Substituted Silver Benzoates.<sup>17,90</sup> The organic acid is dissolved in lot ethanol, and a hot aqueous solution of sodium carbonate is added until the solution is basic to litmus. Nitric acid is then added dropwise until the solution is just acid to litmus. Any solid present is filtered, and a hot aqueous solution of an equivalent amount of silver nitrate is added

to the filtrate. The silver salt is removed by filtration, washed with distilled water and ethanol, and dried at 70°.

Silver Bicyclo[3.3.1]nonan-9-one-1-carboxylate.<sup>71</sup> A solution of 20 g. of bicyclo[3.3.1]nonan-9-one-1-carboxylic acid in 50 ml. of methyl alcohol is titrated to the end point of phenolphthalein with a solution of potassium hydroxide in methyl alcohol. A solution of 18.6 g. of silver nitrate in 20 ml. of water and 50 ml. of methyl alchol is added dropwise with stirring; the silver salt is collected on a filter, washed with methyl alcohol, and dried at 70° under vacuum for eighteen hours. The product contains potassium nitrate but gives results in subsequent reaction that are as satisfactory as those obtained with the silver salt prepared in aqueous solution.

Silver Undecafluorocyclohexanecarboxylate.<sup>76</sup> To a solution of 9.05 g. of undecafluorocyclohexanecarboxylic acid in 66 ml. of perfluorobutyl ether is added 3.22 g. of alkali-free silver oxide. The mixture is shaken intermittently in the dark over a three-day period. Only a trace of unreacted silver oxide remains. The silver salt, 11.35 g. (94.3%), is collected on a Pyrex filter cone, washed with perfluorobutyl ether, and dried at 50° for ten hours. The salt is a white, light-sensitive, crystalline, non-hygroscopic material, soluble in water. All operations in its preparation are carried out in the dark.

### Products Formed by the Hunsdiecker Reaction

Methyl 5-Bromovalerate. The preparation of this material in 52-54% yield from methyl hydrogen adipate is described in Organic Syntheses. 60

n-Propyl Bromide.<sup>20</sup> A solution of 40 g. of bromine in 250 ml. of freshly distilled nitrobenzene is added with vigorous shaking and cooling to 53.5 g. of silver butyrate. In about one minute, the bromine has reacted and the solution is yellow in color. This is followed by sudden, turbulent evolution of earbon dioxide, and the solution becomes quite warm. When gas evolution ceases, the silver bromide is removed by filtration and the filtrate is distilled through a Widmer column. There is obtained 17.2 g. (61%) of n-propyl bromide, 2.7 g. of butyrie acid, and a trace (0.5 g.) of n-propyl butyrate.

n-Heptyl Bromide.<sup>4</sup> To a suspension of 102.5 g, of mercuric oetanoate in 100 ml, of carbon disulfide (dried over phosphorus pentoxide) is added dropwise 22 ml, of dry bromine. There is a smooth evolution of carbon dioxide. When the initial reaction has subsided, the mixture is warmed for a short time on the steam bath. The mercuric bromide is removed by filtration and washed well with earbon disulfide. The solvent is removed from the filtrate and washings, and the residue is fractionated

under reduced pressure to yield 55.7 g. (75%) of n-heptyl bromide, b.p.  $74^{\circ}/18$  mm. A higher boiling fraction (133-137°/18 mm.) is octanoic acid (6.1 g., 10%).

n-Undecyl Bromide.<sup>54</sup> To a suspension of 46 g. of silver laurate in 200 ml. of carbon tetrachloride (dried over phosphorus pentoxide) is added slowly, with stirring and cooling, 7.5 g. of dry bromine in 20 ml. of dry carbon tetrachloride. The mixture is heated gradually until the evolution of carbon dioxide ceases and is then held for a short time at its boiling point. The silver bromide is removed by filtration, placed in an extraction thimble, and extracted for one to two hours, the filtrate being used as an extracting solvent. After the carbon tetrachloride solution is washed with dilute aqueous sodium hydroxide and water, the solvent is removed and the residue distilled to give 24 g. (67%) of undecyl bromide, b.p. 131–134°/15 mm.; 5.5 g. (18%) of lauric acid can be recovered from the alkaline wash liquid.

1,4-Dibromobutane.84 To a well-stirred solution of 48 ml. of dry bromine in 250 ml. of dry carbon tetrachloride is added (with the exclusion of water) 163 g. of silver adipate. The addition is made in small portions over a seven-hour period. After the addition of each portion of silver salt, the reaction is started by warming to 50° and is allowed to continue until the evolution of carbon dioxide ceases. Heating is continued for one-half hour to complete the reaction. The silver bromide is removed by filtration and washed thoroughly with ether. The carbon tetrachloride and ether solutions are combined and decolorized by shaking with a saturated solution of sodium bisulfite; the decolorized solution is shaken with 10% aqueous potassium hydroxide solution, any emulsion that forms being broken with sodium chloride. The solution is finally washed with sodium chloride solution and dried. The solvents are removed through a fractionating column at ordinary pressure, and the The 1,4-dibromobutane distils at 78-81°/11 mm.: residue is distilled. the yield is 58 g. (58%).

1,10-Dibromodecane.<sup>3</sup> A mixture of 40 g. of the silver salt of dodecanedicarboxylic acid and 100 ml. of carbon tetrachloride is treated gradually with 9 ml. of bromine. The silver bromide that separates during the reaction is removed by filtration and washed with hot carbon tetrachloride. The filtrate and washings are combined and shaken with sodium bicarbonate solution to remove any free acid. The solvent is removed and the residue distilled to give 16.8 g. (about 60%) of 1,10-dibromodecane, b.p. 190-195°, m.p. 35-36°.

Methyl 17-Bromoheptadecanoate.<sup>4</sup> To a suspension of 673 g. of the silver salt of methyl 17-carboxyheptadecanoate in 750 ml. of carbon tetrachloride is added, with cooling and stirring, 81 ml. of bromine.

The mixture is finally warmed on a water bath for a short time, and the silver bromide formed is removed by filtration. When the filtrate is cooled to 0°, 58 g. of the monoester acid separates. The remainder can be removed by shaking the solution with dry potassium carbonate; aqueous alkalies form emulsions that are difficult to deal with. Removal of solvent and distillation gives 432 g. (75%) of methyl 17-bromoheptadecanoate, b.p. 212-214°/2.5 mm.

Trifluoromethyl Iodide. A mixture of 66 g. (0.3 mole) of finely ground silver trifluoroacetate and 81 g. (0.32 mole) of powdered iodine was placed in a horizontally held tube, 25 mm. in diameter and 25 cm. long; this tube was sealed at one end while the other end was connected to a wide trap cooled in ice water and backed by two traps cooled in solid earbon dioxide (Dry Ice) and a small water bubbler which served to show the rate of evolution of the earbon dioxide. The ice trap collected a fine sublimate of iodine and prevented clogging of the solid carbon dioxide (Dry Ice) traps, the first of which collected practically all of the trifluoromethyl iodide.

The mixture of silver salt and iodine was heated eautiously with a gas burner, starting at the closed end. The decomposition is smooth at about 100°, but tends to propagate spontaneously and escape control when the heating is not done patiently. The bubbling of earbon dioxide is used as an indicator for the speed at which the burner can be moved along the tube. With the small equipment used, it took ninety minutes to complete the reaction. The crude trifluoromethyl iodide amounted to 47 g. (85%). A scries of larger runs gave an average yield of 87%. Fractional distillation gave a product boiling at 21.8°.

Trifluoromethyliodide is conveniently stored in glass ampules. Exposed to light, it slowly becomes pink, then purple.

A comparable procedure is described by Haszeldine. 78

Cyclobutyl Bromide.<sup>35</sup> To a flask equipped with a mereury-seal stirrer is added 560 ml. of earbon tetraehloride (dried over phosphorus pentoxide), and 50 ml. of earbon tetraehloride is distilled in order to dry the flask thoroughly. The system is protected with a drying tube and, after addition of 85.2 g. (0.534 mole) of bromine (dried over phosphorus pentoxide), the mixture is cooled to -25° with stirring. To this is added 111 g. (0.534 mole) of the silver salt of cyclobutancearboxylic acid. The salt is added over a period of about fifty minutes through a wide rubber connection from the flask in which it had been dried. After an induction period of five to twenty minutes, a vigorous evolution of carbon dioxide sets in and continues as the remainder of the silver salt is added. Evolution of carbon dioxide is accompanied by the evolution of heat, but the temperature is easily maintained at -25 to -20° with a solid carbon

dioxide-acetone bath. After addition is complete, the mixture is stirred briefly until gas evolution becomes slow and then is allowed to warm to room temperature with stirring. When gas evolution has ceased, the silver bromide is removed and washed with carbon tetrachloride. filtrate is washed with 2 N sodium hydroxide and water and then dried over ealcium chloride. The combined alkaline extracts from a total of 2.6 moles of silver salt yield only 2.2 g. of acidic material.

The earbon tetrachloride solution is flash-distilled through a 1-meter column packed with glass helices and equipped with heated jacket and partial reflux head. During flash distillation, the volume of solution in the distilling flask is kept sufficiently large so that the mole fraction of cyclobutyl bromide is kept below 0.2. This avoids loss of bromide, and the carbon tetrachloride is collected at 76.9°. After all the carbon tetrachloride solution has been added, removal of solvent is continued and an intermediate fraction (7.9 g.), b.p. 76.9-108.2°, is collected. Cyclobutyl bromide (36 g., 50%) is collected at 108.2–108.3°;  $n_D^{20}$  1.4801,  $d^{20}$  1.434, MR<sub>D</sub> 26.75 (calculated 26.72). There is 15 g. of distillation residue. By redistilling the intermediate fractions from several runs and stripping the residues in a vacuum, the total yield is raised to 53%. The same yield is obtained in larger (1.9 mole) runs.

p-Nitrobromobenzene. 16 To a suspension of 34 g. of silver p-nitrobenzoate in 500 ml. of carbon tetrachloride 20 g. of bromine is added dropwise at room temperature. The deep-red solution obtained at the end of the addition is heated slowly to boiling; there is no evolution of carbon dioxide below the reflux temperature. The solution is boiled for three hours, during which time the color gradually fades. solution is filtered, and the filtrate is washed with sodium bisulfite and sodium biearbonate solutions. Acidification of the sodium bicarbonate extract produces 2 g. (10%) of p-nitrobenzoic acid. Evaporation of the carbon tetraehloride leaves 20 g. (74%) of crystalline p-nitrobromobenzene, m.p. 126-127°.

Ethyl  $\alpha$ -Bromo- $\beta$ -phenylpropionate.<sup>82</sup> To a solution of 37.5 g. (0.15 mole) of diethyl benzylmalonate in 100 ml. of absolute ethanol is added, with stirring, a solution of 8.7 g. (0.15 mole) of potassium hydroxide in 100 ml. of absolute ethanol. The solution is allowed to stand at room temperature for four to twelve hours; the pH of the final mixture has a value between 7 and 8. Any solids that have formed (assumed to be the dipotassium salt) are removed by filtration. The ethanol is distilled until a thick syrup remains. The last traces of ethanol are removed in vacuum, and the resulting crystals of the potassium salt of the half ester of benzylmalonic acid are placed in a vacuum desiccator for twelve hours.

The dried, finely powdered potassium salt is mixed with 100 ml. of

carbon tetrachloride. The ice-cold mixture is stirred vigorously while a solution of 25 g. (0.15 mole) of bromine in 50 ml. of carbon tetrachloride is added dropwise over a period of two to four hours. The bromine is decolorized rapidly at the start of the reaction, but persists after all of the bromine solution has been added. The mixture is filtered, and the solvent is removed in a current of air. The residue is distilled under reduced pressure to give colorless, strongly lachrymatory ethyl  $\alpha$ -bromo- $\beta$ -phenyl-propionate 38 g. (80%), b.p. 155–159°/15 mm.

### Products Formed by the Simonini Reaction

Because the esters produced by the Simonini reaction are usually procured more easily by other procedures, the reaction has not been developed as a synthetic method. Consequently, no detailed procedure is available. The following example is typical of the experimental work on this reaction.

Benzyl Phenylacetate.<sup>49</sup> When 24.3 g. of silver phenylacetate and 12.7 g. of iodine are mixed in ether, an exothermic reaction sets in and the ether boils. The solvent is removed by distillation and the residue heated for one hour at 80°. The residue is extracted with ether from which 1.35 g. (10%) of phenylacetic acid and 9.35 g. (68%) of benzyl phenylacetate are obtained.

## Products Formed by the Prévost Reaction

2-Iodocyclohexyl Acetate.<sup>21</sup> To 8.2 g. (0.1 mole) of cyclohexene in ether is added 25.4 g. (0.1 mole) of iodine and 16.6 g. (0.1 mole) of silver acetate. An exothermic reaction ensues, and the ether begins to boil. The removed, and the residue fractionated by filtration, the solvent acetate, obtained in 80% yield, boils at 120°/12 mm.

3-Phenyl-1,2-propyleneglycol Dibenzoate. To 11.8 g. of allylbenzene in 300 ml. of dry benzene is added 45.8 g. of silver benzoate and 25.4 g. of iodine (or the corresponding amount of the silver benzoate iodine complex). This mixture is heated under reflux for fifteen hours with the careful exclusion of moisture. The reaction mixture is cooled, washed several times with aqueous sodium bicarbonate solution and reddish-brown residue crystallized in an ice-salt bath. Trituration with collected on a filter, washed with petroleum ether, and dried. The yield of crude product melting at 70-71° is 28.5 g. (85%). The pure product

melts at 74-75°. Hydrolysis to the glycol in a yield of about 85 effected with sodium hydroxide.

1,2-Hexadecanediol.<sup>99</sup> Iodine (10.6 g.) in 100 ml. of dry ben is added, with shaking, to a suspension of 26.5 g. of silver benzoal 150 ml. of benzene. To this solution is added, slowly and with shak 10.5 g. of 1-hexadecene in 50 ml. of benzene. The mixture is he under reflux for one hour, cooled, and filtered, and the filtrate free solvent. The residual glycol dibenzoate is saponified by heating unreflux for three hours with 12 g. of potassium hydroxide in 75 ml ethanol and 25 ml. of water. The glycol is recovered by pouring hydrolysate into 500 ml. of hot water. After cooling, the crude glycollected, recrystallized twice from methanol, then from ligroin (60-70°), and finally from methanol to give 4 g. (33%) of 1,2-hexadecaned m.p. 73-73.6°.

By a similar procedure, 288 g. of 1-octadecene, 620 g. of silver benzon and 290 g. of iodine give 239 g. (73%) of 1,2-octadecanediol, m. 79-79.5°.

2-Bromocyclohexyl Benzoate.<sup>22</sup> To a suspension of 11 g. of silbenzoate in 75 ml. of carbon tetrachloride cooled to -10° is added one-hof a solution of 7.3 g. of bromine in 18 ml. of carbon tetrachloride a one-half of a solution of 3.8. g of cyclohexene in 15 ml. of the same solve After ten or fifteen minutes, the remainder of the bromine and cyclohexe solutions is added. The precipitate is removed by filtration and wash with carbon tetrachloride. The combined filtrates are washed first wi dilute aqueous sodium hydroxide to remove any benzoic acid and the with water. The solution is dried over calcium chloride, the solvent removed, and the residue is recrystallized from petroleum ether. The product (42%) melts at 64-64.5°.

# Products Formed by Substitution Reactions of Acyl Hypohalites

 $\beta$ -(2-Iodo-5-methoxyphenyl)propionic Acid. Method 1.<sup>18</sup> To stirred solution of 0.1 mole of  $\beta$ -(3-methoxyphenyl)propionic acid in 10 ml. of acetic acid there is added alternately, in small portions, 25.4 g (0.1 mole) of powdered iodine and 16.6 g. (0.1 mole) of silver acetate Iodination proceeds rapidly at room temperature. The iodinated mixtures stirred for one hour at room temperature after the addition is complete iltered, and the filtrate is diluted with water. The oily product that separates is extracted with ether, the other extracts are washed free or acetic acid, and the iodinated acid is purified by recrystallization from a nixture of chloroform and petroleum ether. The product obtained in 30% yield melts at 109-110°.

Method II.<sup>18</sup> To a suspension of 14.3 g. (0.05 mole) of silver  $\beta$ -(3-methoxyphenyl)propionate in 100 ml. of anhydrous carbon tetrachloride in a 500-ml. three-necked flask equipped with an efficient stirrer, there is added dropwise at room temperature 25.4 g. (0.1 mole) of iodine dissolved in carbon tetrachloride. The iodine reacts immediately and silver iodide precipitates. After the addition is complete, the mixture is stirred for one hour, the silver iodide is separated, and the solvent is removed under reduced pressure. The iodinated acid is purified by crystallization from chloroform-petroleum ether. The yield is 90%, m.p. 109–110°.

p-Diiodobenzene.<sup>19</sup> A mixture of 12 ml. (0.11 mole) of iodobenzene and 4.4 g. (0.02 mole) of silver trifluoroacetate is heated to 100° in a small flask fitted with a condenser which is connected by rubber tubing to liquid air traps. The mixture is cooled to room temperature and 5.1 g. (0.02 mole) of powdered iodine is added. There is an immediate precipitation of silver iodide. The mixture is heated rapidly to 160°, cooled to room temperature, and filtered. The liquid air traps contain only a small amount of trifluoroacetic acid. Distillation of the solution gives 1.85 g. (80%) of trifluoroacetic acid, b.p. 71–72°, iodobenzene, b.p. 80°/12 mm., and 5.1 g. (77%) of p-diiodobenzene, which may be crystallized from ethanol as plates, m.p. 128°.

4-Iodoveratrole.<sup>53a</sup> A mixture of 110 g. (0.5 mole) of silver trifluoroacetate and 69 g. (0.5 mole) of dry veratrole was placed in a dry, 1-l. flask equipped with stirrer and dropping funnel. A chloroform solution of iodine was prepared from 127 g. (0.5 mole) of iodine and about 750 ml. of chloroform. The chloroform solution was added during one-half hour, after which any undissolved iodine was added as the solid. (Alternatively, sufficient chloroform to dissolve the iodine, about 15:1, may be used.) After stirring for two hours, the mixture was filtered and the precipitate washed with 100 ml. of chloroform. The solvent was removed and the residue distilled. The yield of product boiling at 152–155°/15 mm. was 112 g. (85%). Redistillation gave a pale-yellow product,  $n_D^{e5}$  1.6117, which after crystallization from ethanol melted at 34–35°.

### TABULAR SURVEY OF SILVER SALT-HALOGEN REACTIONS

In Tables I-XVII are listed all the examples of silver salt-halogen reactions that have been noted in a survey of the literature through 1954.\* In general, the substances are arranged in increasing order of molecular weight. Most of the tables provide the following information: silver salt employed, solvent, main product of the reaction, yield, and reference. A separate column for the halogen used is not included since the formula of the product will make this clear.

<sup>\*</sup> The bibliography in reference 2a covers the literature through June 1955.

28

FORMATION OF ALKYL HALIDES FROM ALIPHATIC MONOCARBOXYLIC ACIDS

မွ

Aeid	Solvent	Main Produet	Yield, %	Referenc
CH <sub>3</sub> CO <sub>2</sub> H	None	CH,Br	1	56
1	None	$CH_1Br$	80	က
	CCI4	CHABr	69	20
$^{n}$ - $\mathrm{C_{3}H_{7}CO_{2}H}$	$c_{ m eH_5NO_2}$	$n\text{-}\mathrm{C_3H_7Br}$	61	20
$^{n\cdot C_4H_3CO_2H}$	CS <sub>2</sub>	$n\text{-}\mathrm{C}_4\mathbf{H}_9\mathbf{Br}$	31	25
$C_2II_5CH(CH_3)CO_2H^*$	$C_6H_5NO_2$	$C_2H_5$ CHCICH $_3$	74 erude	25
	$CS_2$	$C_2H_5CHBrCH_3$	14	25
$(CH_3)_3CCO_2H$	$CS_2$	No definite products		25
(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub> CO <sub>2</sub> H	$CS_2$	$(CH_3)_2 CH CH_3 Br$	15	25
$n$ - $C_5$ H $_{11}$ CO $_2$ H	CCI <sub>4</sub>	n-C <sub>5</sub> H <sub>1</sub> ·Br	92†	63
n-C <sub>3</sub> H,CH(CH <sub>3</sub> )CO <sub>2</sub> H	CCI	n-C,H,CHBrCH,	55-65	99
(C2H5)2CHCO2H	CCI⁴	$(C_2H_5)$ ,CHBr	76	99
(CII3)2CHCH2CH2CO2H	CS <sub>2</sub>	$(CH_3)_2CHCH_2CH_2B_\Gamma$	42	25
(Cura)acchacoah	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	$(\mathrm{CH_3})_3\mathrm{CCH_2Br}$	62	33
n.C. HCO. H	cci.	$(CH_3)_3CCH_2Br$	83†	63
"-C.H.CH/C H VCO H+		$n ext{-} ext{C}_7 ext{H}_{15} ext{Br}$	19	30
+11200(21120)11001110	CCI	$n\text{-}\mathrm{C}_4\mathrm{H}_9\mathrm{CHBrC}_2\mathrm{H}_5\S$	30-50	94, 96, 9
* The (+) acid gives an optically inactive chloride,	stically inactive chloride.	•		
***				

ho yield is not based on pure isolated material, but on a quantitative determination of bromine present in the neutral fraction of the reaction product.

‡ The silver salt was added to bromino in carbon tetrachloride, the reverse of the normal addition. § Both optically active forms of the silver salt gave the optically inactive bromide. However, in reference 28 it is reported that the bromido from silver (+)-2-ethylhexanoate had some optical activity.

TABLE I-Continued

		Reference	3, 54, 55	ಣ	œ	œ	œ	63	55, 58	87	87	87	3, 55, 87	87	3	55, 63	20	87	00	
•	Tric Acids	Yield, %	59-80	75-80	51-65	72-87	70-78	499	65-77: 70	51	5 6	0£	70-80	15-47	Variable	73-86: 89‡	38 crude	. 09	) u	00
	HATIMES PROM ALIPHATIC MONOCARBOXYLIC ACIDS		Main Product	$n ext{-}\mathrm{C}_{11}\mathrm{H}_{23}\mathrm{Br}$	$n ext{-}\mathrm{C}_{11}\mathrm{H}_{23}\mathrm{Br}$	$n\text{-}\mathrm{C}_{11}\mathrm{H}_{23}\mathrm{I}$	$n\text{-}\mathrm{C}_{11}\mathrm{H}_{23}\mathrm{I}$	$n\text{-}\mathrm{C}_{11}\mathrm{H}_{23}\mathrm{I}$	$(i\cdot \mathrm{C_5H_{11}})_2\mathrm{CHBr}$	$n ext{-}\mathrm{C}_{13}\mathrm{H}_{27}\mathrm{Br}$	$n ext{-}\mathrm{C}_{13}\mathrm{H}_{27}\mathrm{I}$	$n$ -C <sub>15</sub> $\mathbf{H_{31}}^{\mathrm{Cl}}$	$n$ - $\mathbf{C_{15}H_{31}^{Cl}}$	$n ext{-}\mathrm{C}_{15}\mathrm{H}_{31}\mathrm{Br}$	$n$ - $\mathrm{C}_{15}\mathrm{H}_{31}\mathrm{I}$	$n$ - $\mathbf{C_{17}H_{35}^{Cl}}$	$n$ - $\mathrm{C}_{17}\mathrm{H}_{35}\mathrm{Br}$	$n$ - $\mathrm{C_{17}H_{35}Br}$	$n ext{-} ext{C}_{f 17} ext{H}_{f 35} ext{I}$	$n ext{-} ext{C}_{17} ext{H}_{35} ext{I}$
	MILL TO THE PARTY OF THE PARTY	FORMATION OF ALKYL HALLE	Solvent	ממן,	CHCI	Pet, ether	C,H,	100	, CC.	מסוי,		CO	C,H,CI,		COI	None	CCI	CCI	. 50	C,H,
			177	Acid	$n.\mathrm{C_{11}H_{23}CO_{2}H}$					$(i.C_5H_{11})_2$ CHCO $_2$ H	$n$ - $\mathrm{C}_{13}\mathrm{H}_{27}\mathrm{CO}_2\mathrm{H}$	\$	$n \cdot \mathrm{C_{15}H_{31}CO_{2}H}$			H OV H V	$n \cdot c_{17}$ $n_{35}$ $co_2$ $t_1$			

† The yield is not based on pure isolated material, but on a quantitative determination of bromine present in the neutral fraction of the reaction mixture.

TABLE II FORMATION OF ALKYL HALIDES FROM PHENYL-SUBSTITUTED CARBOXYLIC ACIDS Unless otherwise indicated, the solvent was carbon tetrachloride.

			40.
Acid	Main Product	Yield, %	Reference
$\mathrm{C_6H_5CH_2CO_2H}$	$\mathrm{C_6H_5CH_2Br}$	54*	63
	$\mathrm{C_6H_5CH_2Br}$	20-37†	25
$p ext{-}\mathrm{O_2NC_6H_4CH_2CO_2H}$	$p\text{-}\mathrm{O_2NC_6H_4CH_2Br}$	85	16
$(\mathrm{C_6H_5)_2CHCO_2H}$	$(\mathrm{C_6H_5})_2\mathrm{CHBr}$	8	25
$(\mathrm{C_6H_5})_3\mathrm{CCO_2H}$	$(\mathrm{C_6H_5})_3\mathrm{COH}$	8	25
$\mathrm{CH_3CH(C_6H_5)CO_2H}$	$\mathrm{CH_3CHBrC_6H_5}$	-‡	27
$\mathrm{C_{6}H_{5}CH_{2}CH_{2}CO_{2}H}$	$\mathrm{C_6H_5CH_2CH_2Br}$	5-15	16, 25
$p\text{-}\mathrm{O_2NC_6H_4CH_2CH_2CO_2H}$	$p\text{-}\mathrm{O_2NC_6H_4CH_2CH_2Br}$	80	16
$\mathrm{C_6H_5CH_2CH(C_6H_5)CO_2H}$	$\mathrm{C_6H_5CHBrCHBrC_6H_5}$	52	16
$(+) \cdot \mathrm{C_6H_5CH_2CH}(\mathrm{C_2H_5})\mathrm{CO_2H}$	$(+,-)\text{-}\mathrm{C}_6\mathrm{H}_5\mathrm{CH}_2\mathrm{CHBrC}_2\mathrm{H}_5$	17	26
$(-)\text{-}\mathrm{C_6H_5CH_2CH}(\mathrm{C_2H_5})\mathrm{CO_2H}$	$(+,-)\text{-}\mathrm{C}_6\mathrm{H}_5\mathrm{CH}_2\mathrm{CHBrC}_2\mathrm{H}_5$	_	26
$^{\mathrm{C}_{6}\mathrm{H}_{5}\mathrm{C}}\!\!\!\!=\!$	$C_6H_5C\equiv CI$	94	49

<sup>\*</sup> This yield is based on a quantitative determination of bromine present in the neutral fraction of the reaction mixture and not on pure isolated material.

tral fraction of the reaction mixture and not on the reverse of the the reverse of the the silver salt was added to bromine in carbon tetrachloride, the reverse of the normal procedure.

The solvent used in this experiment was benzene.

rmal procedure.

1 It was originally reported 27 that 1-bromo-1-phenylethane was obtained in 55% ‡ It was originally reported 27 that 1-promotion and, in attempts to repeat yield. Other chemists 33,85 could not obtain this product, and, in attempts to repeat no allest or repeat yield. Other chemists<sup>83,85</sup> could not obtain this provided failure;<sup>28</sup> no alkyl bromido was obtained.

<sup>§</sup> Although no identifiable substances were isolated from the products resulting § Although no identifiable substances were isolated from the action of iodine on silver cinnamate or silver crotonate, silver resulting from the action of iodine on silver cinnamate or silver crotonate, silver phenylfrom the action of iodine on silver communated. A small amount of triiodostyrene was formed simultaneously.

TABLE III

FORMATION OF HALIDES AND/OR LACTONES FROM DICARBONYLIC ACIDS

Unless otherwise indicated, the solvent was carbon tetrachloride.

Acid	Main Product	Yield, %	Reference
	Br(CH <sub>2</sub> ) <sub>2</sub> Br	32-37†	40, 85
22 2 10 ( - 22 12 - 22 -	OCCH,CH,CH,O	69‡	63
THE GOTTING TO LOCATE	OH OHD- S	28	40
	C <sub>2</sub> H <sub>5</sub> CHBr <sub>2</sub> §	12	63
HO <sub>2</sub> CCH <sub>2</sub> CH(CH <sub>2</sub> )CO <sub>2</sub> H	BrCH <sub>2</sub> CHBrCH <sub>3</sub>		20
HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> CO <sub>2</sub> H	Br(CH <sub>2</sub> ) <sub>4</sub> Br	Small	
	Br(CH <sub>2</sub> ) <sub>4</sub> Br	21	54
	Br(CH <sub>2</sub> ) <sub>4</sub> Br*	58	84
	Br(CH <sub>2</sub> ) <sub>4</sub> Br	28	63
$\mathrm{HO_{2}C(CH_{2})_{2}CH(CH_{3})CO_{2}H}$	occh.ch.ch(ch.)o¶	87‡	63
HO,C(CH,),CO,H	Br(CH <sub>2</sub> ) <sub>5</sub> Br	44 ‡	63
HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> CO <sub>2</sub> H	OCCH_CH_C(CH_3)_O¶	50‡	63
2-HO <sub>2</sub> CC <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> H	2-BrC <sub>6</sub> H <sub>4</sub> Br	10	63
3.HO2CC'H'CO'H	3-BrC <sub>6</sub> H <sub>4</sub> Br**	4	63
4-HO <sub>2</sub> CC <sub>4</sub> H <sub>4</sub> CO <sub>2</sub> H	• •	**	63
HO,C(CH,),CO,H	Br(CH <sub>2</sub> ) <sub>7</sub> Br	82‡	63
$\mathrm{HO_{2}CCH_{2}CH(C_{3}H_{11}\text{-}i)CO_{2}H}$	BrCH <sub>2</sub> CHBrC <sub>5</sub> H <sub>11</sub> -i	25‡	63
HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> H	Br(CH <sub>2</sub> ) <sub>8</sub> Br	62-81	3, 54, 63
$\mathrm{HO_2C(CH_2)_2CH(C_3H_{11}\cdot i)CO_2H}$	OCCH,CH,CH(C,H,,-i)O	¶ 60‡	63
HO,CC(CH,),CH(C,H,,-i)CO,H	Br(CH <sub>2</sub> ) <sub>3</sub> CHBrC <sub>5</sub> H <sub>11</sub> -i	33‡	63
HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>10</sub> CO <sub>2</sub> H	Br(CH <sub>2</sub> ) <sub>10</sub> Br	60	3
HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>14</sub> CO <sub>2</sub> H	Br(CH <sub>2</sub> ) <sub>14</sub> Br	44	54
C.H.CH(CO.H)CH(CO.H)C.Hs	C.H.CHBrCHBrC.H.	High	26
HO,C(CH,),CH(CO,H)CH,CO,E		4-6	40

TABLE IV

FORMATION OF HALO ESTERS FROM ACID ESTERS

Unless otherwise indicated, the solvent was carbon tetrachloride.

Silver Salt of Acid	Main Product	Yield, %	Reference
CH <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> CO <sub>2</sub> H	CH <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> Br	65-68	4, 60, 61
CH2O2C(CH2)6CO2H	CH <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>6</sub> Br	70	4
$\mathrm{CH_2O_2C(CH_2)_7CO_2H}$	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>7</sub> Br	70	4
$\mathrm{CH_3O_2C(CH_2)_8CO_2H}$	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>8</sub> Br	75	3, 4
$\mathrm{CH_{2}O_{2}C(CH_{2})_{9}CO_{2}H}$	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>9</sub> Br	71	3, 4
$\mathrm{CH_3O_2C(CH_2)_{11}CO_2H}$	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>11</sub> Br	78	4
CH <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>12</sub> CO <sub>2</sub> H	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>12</sub> Br	71	4
CH <sub>2</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>13</sub> CO <sub>2</sub> H	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>13</sub> Br	73	4
$\mathrm{CH_{2}O_{2}C(CH_{2})_{14}CO_{2}H}$	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>14</sub> Br	70 (65–70)	4, 62
	CH <sub>3</sub> O <sub>2</sub> C(CH <sub>2</sub> ) <sub>14</sub> Br	78-85*	62
$\mathrm{CH_{2}O_{2}C(CH_{2})_{15}CO_{2}H}$	$\mathrm{CH_3O_2C(CH_2)_{15}Br}$	70	4
$\mathrm{CH_2O_2C(CH_2)_{16}CO_2H}$	$\mathrm{CH_2O_2C(CH_2)_{16}Br}$	75	4
CH2-CH2	CH2-CH2		
CHCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	CH <sub>2</sub> CHCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	68-72	5
CH2-CHCO2H	CH <sub>2</sub> —CHBr		

<sup>\*</sup> The solvent in this experiment was trichloroethylene.

TABLE V

FORMATION OF ALKYL HALIDES FROM POLYHALO AND PERFLUORO AGIDS\*

Acid	Product	Yield, %	Reference
	CH <sub>2</sub> FCl	52	73
$\mathrm{CH_2FCO_2H}$	_	62	73
	CH <sub>2</sub> FBr	55	73
	CH <sub>2</sub> FI	73	73
$\mathrm{CHFClCO_2H}$	CHFCl <sub>2</sub>	67	73
	CHFClBr	35	73
	CHFCII	67	73
$\mathrm{CHFBrCO}_{2}\mathrm{H}$	CHFBrCl		73
	$\mathrm{CHFBr}_2$	64	73
	CHFBrI	19	73
$\mathrm{CHFICO_2H}$	$\mathrm{CHFI}_2$	18	73
$\mathrm{CHF_2CO_2H}$	$\mathrm{CHF_2Cl}$	91	73
	$\mathrm{CHF}_2\mathrm{Br}$	88-93	73 73
	$\mathtt{CHF_2I}$	93	73 73
$\mathrm{CFClBrCO_2H}$	$\mathrm{CFCl_2Br}$	63	
	$CFClBr_2$	71	73
CFCl <sub>2</sub> CO <sub>2</sub> H mixture	CFCl <sub>3</sub>	63	73 73
CHFCICO <sub>2</sub> H	$CHFCl_2$	78	73
	$\mathrm{CFCl_2Br}$	58	73
	CHFCiBr	61	73 73
	$CFCl_2I$	10	73 73
	CHFCII	29	
$\mathrm{CF_2BrCO_2H}$	$\mathbf{CF_2Br_2}$	81	73
$\mathrm{CF_2ClCO_2H}$	$\mathbf{CF_2Cl_2}$	88	73
	${ m CF}_2{ m ClBr}$	91	73 -2
	$ ext{CF}_2 ext{ClI}$	78	73
$\rm CCl_3CO_2H$		<del></del>	49

<sup>\*</sup> Unless otherwise specified, the reactions with chlorine and bromine were carried out in sealed tubes or in a steel autoclave without a solvent; with iodine an intimate mixture of the halogen and silver salt was heated in an open flask.

TABLE V—Continued FORMATION OF ALKYL HALIDES FROM POLYHALO AND PERFLUORO ACIDS

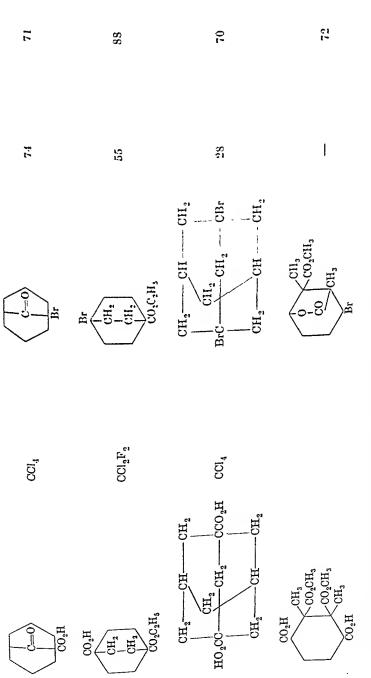
Acid	Product	Yield, %	Reference
$\mathrm{CF_3CO_2H}$	CF <sub>3</sub> Cl	90; 88	78, 79
	$\mathrm{CF_3^2Br}$	88; 98	78, 79
	$\mathrm{CF_3^I}$	87-95	74, 77, 78
$^{\mathrm{C_2F_5CO_2H}}$	$\mathrm{C_2F_5Cl}$	94; 83	73, 79
	$\mathrm{C_2F_5Br}$	98; 98	73, 79
	$C_2F_5I$	94; 86	73, 74
$^{n\text{-}\mathrm{C}_3\mathrm{F}_7\mathrm{CO}_2\mathrm{H}}$	$n ext{-}\mathrm{C}_3\mathrm{F}_7\mathrm{Cl}$	91; 71	73, 79
	$n ext{-}\mathrm{C_3F_7Br}$	97; 95	73, 79
	$n$ -C $_3$ F $_7$ I	90; 86-93	73, 74, 80
$^{n ext{-}\mathrm{C_4F_9CO_2H}}$	$n ext{-}\mathrm{C_4F_9Cl}$	89	73
	$n ext{-}\mathrm{C_4F_9Br}$	95	73
	$n ext{-}\mathrm{C_4F_9I}$	89	73
$n$ -C $_5$ F $_{11}$ CO $_2$ H	$n ext{-} ext{C}_5 ext{F}_{11} ext{Cl}$	85; 71	73, 75
	$n ext{-} ext{C}_5 ext{F}_{11} ext{Br}$	91; 83	73, 75
	$n ext{-} ext{C}_5 ext{F}_{11} ext{I}$	89; 74	73, 75
$^{n ext{-}\mathrm{C}_6\mathrm{F}_{13}\mathrm{CO}_2\mathrm{H}}$	$n ext{-} ext{C}_6 ext{F}_{13} ext{CI}$	83	73
	$n ext{-}\mathrm{C_6F_{13}Br}$	90	73
	$n ext{-}\mathrm{C_6F_{13}I}$	90	73
$^{n\text{-}\mathrm{C}_7\mathrm{F}_{15}\mathrm{CO}_2\mathrm{H}}$	$n ext{-} ext{C}_{7} ext{F}_{15} ext{Cl}$	80	73
	$n ext{-}\mathrm{C_7F_{15}Br}$	86	73
	$n ext{-}\mathrm{C_7F_{15}I}$	85	73
$\mathrm{HO_{2}C(CF_{2})_{3}CO_{2}H}$	$\mathrm{Cl}(\mathrm{CF}_2)_3\mathrm{Cl}$	64	86
<del>.</del>	$\mathrm{Br}(\mathrm{CF}_2)_3\mathrm{Br}$	80	86
OTT	$I(CF_2)_3I$	18†	74, 86
$^{\mathrm{CF}_2-\mathrm{CF}_2}$			m.c
CFCO <sub>2</sub> H	$\mathrm{C_6F_{11}Br}_{7}^{+}$	54	76
$CF_2$ $CFCO_2H$ $CF_2$ $CF_2$	$C_6F_{11}I$ ‡	63	76
		bustsmolaatona	

<sup>†</sup> The main product of the reaction is perfluorobutyrolactone. ‡ Perfluorotributylamine was used as a solvent.

68, 69 Reference 37 35, 48 37 37 66 73-80; 57 ‡09 Yiold, % 58‡ ١ 50‡ 73-80 50, 57 15-2055 FORMATION OF ALICYCLIC BROMIDES FROM ALICYCLIC CARBOXYLIC ACIDS 53 CH2(CH2)2CHBr\*† Main Product CH2(CH2)3CHBr CH2(CH2)4CHBr ÇH2(CH2)5CHBr CH2(CH2)4CHCI CH2CH2CHBr\* CH2CH2CHBr н,ссси, TABLE VI CCl4 (high temp.) CCl4 (low temp.) Solvent  $CCl_4$ ,  $CF_2Cl_2$ Pet, ether ١  $C_2H_2Cl_2$  $\mathrm{CCl}_2\mathrm{F}_2$ CCI<sup>‡</sup> CCI₄ CCI CH2(CH2)4CHCO2H CH2(CH2)5CHCO2H CH2(CH2)3CHCO2H  $\mathrm{CH}_2(\mathrm{CH}_2)_2\mathrm{CHCO}_2\mathrm{H}$ CH2CHCO2H Acid

 $CO_2H$ 

H,CCCH,



\* The silver salt was added to the bromine in the solvent at -25 to -35°, the reverse of the normal addition. † This reaction has also been run with the mereuric salt. See Table IX. † The products are mixtures of ehloro- and bromo-apocamphane. Attempts at separation failed.

TABLE VII FORMATION OF ARYL HALIDES FROM AROMATIC CARBONYLIC ACIDS\*

Substituents in Aromatic Acid (Benzoic)	Substituents in Aryl Bromide (Bromobenzene)	Yield, %	Roference
None	None	14–18	16, 20
None	None	46-80	17, 20, 63
2-Chloro	2-Chloro	38	16
z-Chioro	2-0111010	46	17
3-Chloro	3-Chloro	44	16
4-Chloro	4-Chloro	55	16
2-Nitro	2-Nitro	95, 71	16, 63
3-Nitro	3-Nitro	89	16
3-IXIUO	3-141010	68	17
4-Nitro	4-Nitro	79	16
3-Methyl	3-Methyl†	27	17
•	·	17	16
4-Methyl	4-Methyl‡	50	17
3-Methoxy	2-Carboxy-4-methoxy		16
4-Methoxy	3-Bromo-4-methoxy§	19-23	
3-Bromo-4-methoxy	3-Bromo-4-methoxy	92	16

<sup>\*</sup> In all the reactions recorded in this table carbon tetrachloride was used as the solvent.

<sup>† 3,4-</sup>Dibromotoluene was also obtained in 13% yield.

‡ The principal product was 3-bromo-p-toluic acid, obtained in 66% yield.

§ The principal product was 3-bromo-4-methoxybenzoic acid, obtained in 73% yield.

FORMATION OF SUBSTITUTED ALKYL HALIDES OR THEIR DECOMPOSITION PRODUCTS PROM STREET MONOCARROXYLIC ACIDS

TABLE VIII

FR	OM SUBSTITUT	FROM SUBSTITUTED MONOCARBOXYLIC ACIDS		
Acid	Solvent	Product	Yiold, %	Roforonce
$c_{ m o}$ II $_{ m c}$ CIIOHCO $_{ m a}$ H $_{ m i}$ ·C $_{ m I_A}$ II $_{ m 29}$ CIIOIICO $_{ m e}$ H	$A.$ $(C_2H_5)_2O$ Nono	Hydroxy Acids $C_6H_5CHO$ $n\text{-}C_{14}H_{29}CHO$	Variable —	ကက
BrCH2CH2CO2H* CH3(CH2)2CHBrCO2H* n-C10H3nCHBrCO2H n-C41H7(CHCh2(CH2)7CO2H n-C5H1H(CHBr)2CH2(CH2)7CO2H	B. CCI, CCI, CCI, CCI, CCI,	$\begin{aligned} & Halogen\ Acids \\ & \text{Br}(\text{CH}_2)_2\text{Br} \\ & \text{CH}_3(\text{CH}_2)_2\text{CHBr}_2 \\ & n\text{-}C_{16}\text{H}_{33}\text{CHBr}_2 \\ & n\text{-}C_8\text{H}_{17}(\text{CHCl})_2(\text{CH}_2)_7\text{Br} \\ & n\text{-}C_5\text{H}_{11}(\text{CHBr})_2\text{CH}_2(\text{CHBr})_2(\text{CH}_2)_7\text{Br} \end{aligned}$	69 52 70–75 crude 76 crude	40 40 3 3 59
CH3COCO211 CH3CO(CH2)7CO211	, , , , , , , , , ,	$C$ . Keto Acids ${ m CH_3COBr}$ ${ m CH_3CO(CH_2)_7Br}$	30+	63 3
CH <sub>3</sub> CH(NHCOC <sub>6</sub> H <sub>3</sub> )CO <sub>2</sub> H n·C <sub>1</sub> H <sub>3</sub> CH(NHCOCH <sub>3</sub> )CO <sub>2</sub> H C <sub>1</sub> H <sub>3</sub> CH <sub>2</sub> CH(NHCOC <sub>6</sub> H <sub>3</sub> )CO <sub>2</sub> H * The dry silver salt was added to the † The yield is not based on icol. to	D. CH <sub>3</sub> CO <sub>2</sub> H (C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub> O CCl <sub>1</sub> CH <sub>3</sub> CO <sub>2</sub> H	$\begin{array}{llllllllllllllllllllllllllllllllllll$	Variablo Variablo Variable Variablo	8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8

fraction of the reaction mixture,

<sup>#</sup> The substituted alkyl ladides formed from acylated amino acids are highly hygroscopic materials which decompose in water with the formation of aldehyde, anide, and hydrogen bromide. The yields of aldehyde isolated through the dinitro-

10

Robucts		67-73				
TABLE VIII—Communication Products	FORMATION OF NUBSTRICTED ALMYL HARDEN TO FORMATION OF THOM STREETED MONOCARDOXYLIC ACIDS	P. Alicyclic Acetic Acid	ລວ	CHICHICHICHIC CHICAGON R. CHI R."	F. Bile Acids CII3	2 5 cm

Yjold, Refor- % onco	
 Substituents in Product	Solvent R" =

7, Oct. 65	poor 65 64 40 64 89 65a 60 65a 60 64 25 64 — 65a — 65a — 65a — 65a
R'''	H Br CH <sub>3</sub> CO <sub>2</sub> CH(CH <sub>3</sub> )Br CH <sub>3</sub> CO <sub>2</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> Br H CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br H CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br O CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br O CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br CH <sub>3</sub> CO <sub>2</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br CH <sub>3</sub> CO <sub>2</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br CH <sub>3</sub> CO <sub>2</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br CH <sub>3</sub> CO <sub>2</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br CH <sub>3</sub> CO <sub>2</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> CH <sub>2</sub> Br
Solvent R = R' = R" =	CCI, CH3CO2 H CH3CO CCI, CH3CO2 H CH3CO CCI, CH3CO2 H CH3CO CCI, H H H C2, H C CCI, CH3CO2 H CH3CO CCI, CH3CO2 H CH3CO CCI, CH3CO2 H CH3CO CCI, CH3CO2 H CH3CO C2H3Br CH3CO2 CH3CO2 H C2H3Br CA3CO2 CH3CO2 H C2H3Br CA3CO2 CH3CO2 H C2H3Br CCI, ICH3CO2 H
	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

§ The product was amorphous.

FORMATION OF HALOGEN COMPOUNDS BY THE ACTION OF HALOGEN ON VARIOUS METALLIC SALTS TABLE IX

TOWNWIND T		OF CARB	OF CARBOXYLIC ACIDS	•	ç
Acid	Salt	Solvent	Product	Yield, %	Keterence
H OJ HJC	Hg++	CS,	CH,0	08-09	က
CR CO II	*** Z'a*	None	$\text{CF}_{3}$ I	58-61	78
3CO2H	**	None	CF,I	40	73, 78
	Ba*	None	$CF_{i}$	32	78
	H0++*	None	CF,I	35	78
	Pb*	None	$CF_3^{I}$	26	73, 78
H2(CII2)2CHCO2H	$^{+g++}$	$CS_2$	CH2(CH2)2CHBr	45	ιG
H°00°H33°07H°	K	ccı,	C,H,O,CCH,Br	23	82
n.C.11,.CO,H	TI+	CCI,	n-C,H,2	High	က
21 22	$\mathrm{TI}^{+}$	ຸ້ເວວ	$n ext{-}\mathrm{C}_{\mathbf{k}}\mathrm{H}_{13}\mathrm{Br}$	100	က
C2H,O2CCH(C2H5)CO2H	К	CCI <sub>4</sub>	$c_2 \ddot{H_5} O_2 CCHClC_2 H_5$	41	83
•	K	CCI	C_H,O_CCHBrC_H,	36	82
n-C <sub>7</sub> H <sub>15</sub> CO <sub>2</sub> H	K	CCI.	$n$ -C, $\mathbf{H_{15}Br}$	45	4
	$_{ m Hg^+}$	CCI <sup>4</sup>	$n ext{-}\mathrm{C}_7\mathrm{H}_{15}\mathrm{Br}$	09	က
,	$^{ m Hg^+}$	CS,	$n ext{-}\mathrm{C}_7\mathrm{H}_{15}\mathrm{Br}$	75	3, 4
C211,O2CCH(C3H7-i)CO2H	K	CCI,	C2H5O2CCHBrC3H7-i	30	82
$C_2 H_5 O_2 CCH(C_1 H_9 - n) CO_2 H$	¥	CCI⁴	$C_2H_5O_2CCHClC_4H_9$ - $n$	52	83
	ļ		$\mathrm{C_2H_5O_2CCHBrC_4H_9}$ - $n$	29	82
Carls O CCH (Ch. H. 13-7) CO THE	¥ ;	CCI	$\mathrm{C_2H_5O_2CCHClC_6H_{13}}$ - $n$	54	83
Call South (Central) Coald	<b>4</b>		$\mathrm{C_2H_5O_2CCHBrC_6H_{11}}$	45	82
C2115O2CCH(CH2C6H5)CO2H	¥	CC	$\mathrm{C_2H_5O_2CCHBrCH_2C_6H_5}$	80	82
C11 O CC11(C8H17-N)CO2H			$C_2H_5O_2CCHClC_8H_{17}$ -n	20	83
			$\mathrm{C_2H_5O_2CCHClC_{10}H_{21}}$ - $n$	16	83
7.012 113100 git	, Bu	CCI4	$n ext{-}\mathrm{C}_{15}\mathrm{H}_{31}\mathrm{Br}$	02-09	က
* The reaction was earried out in a steel autoclave at 270°.	out in a stee	el autoclave at			

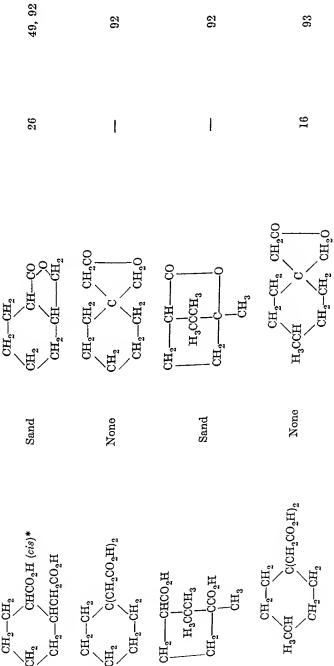
TABLE XI

FORMATION OF ALDEHYDES AND KETONES BY THE ACTION OF IODINE ON THE SILVER SALTS OF HYDROXY ACIDS

Acid	Diluent	Product	Yield, %	Reference
$\mathrm{HOCH_{2}CO_{2}H}$	$\mathrm{C_2H_5OH}$	${ m CH_2O}*$		49, 89
$\mathrm{CH_{2}OHCHOHCO_{2}H}$	Quartz	$\mathrm{CH_2O}*$		89
$\mathrm{CH_{3}CHOHCO_{2}H}$	$\mathrm{C_2H_5OH}$	CH <sub>3</sub> CHO*		49, 89
$\mathrm{C_6H_5CHOHCO_2H}$	$(\mathrm{C_2H_5)_2O}$	${ m C_6H_5CHO}$	60†	49, 89
$(\mathrm{CH_3})_2\mathrm{C(OH)CO_2H}$	$C_2H_5OH$	$(CH_3)_2CO^*$		89
$(\mathrm{C_6H_5)_2C(OH)CO_2H}$	$\mathrm{C_6H_6}$	$\mathrm{C_6H_5COC_6H_5}^{\color{gray}*}$	_	49

<sup>\*</sup> This material was identified as one product of the reaction mixture; no yields were recorded.

† The product was contaminated with benzene which was the solvent used in one case. 49



\* The trans-isomer also gave the cis-lactone, but in a smaller yield.

# TABLE NIII

noid and halogen and was used without isolation. Appition of Acyl, Hypohalites to Olefins

flo neyl lis	The acyl hypedulate was prepared from the silver salt of the acid and independent.	the silver salt of tl o this statement ar	repared from the silver soft of the noid and hungen are. Executions to this statement are indicated by footnotes.	•	Refor-
		Solvent	Product	Yield, % enco	enco
	Acyl Hyponante		040000000000000000000000000000000000000	Good	10
	Carscoal	$C_6H_6$	Ethanedioi dipenzoneo 2-Todocthyl 3,5-dinitrobenzoato	Good	96 10
	3,5.(NO <sub>2</sub> )2C <sub>4</sub> H3CO <sub>2</sub> F C <sub>4</sub> H <sub>5</sub> CO <sub>2</sub> F	C <sub>6</sub> H <sub>6</sub>	1,2.Propanediol dibenzouco 1.1odo-2-propyl 3,5-dinitro-	,	96
	$3,5.(NO_2)_2C_0\Pi_3CO_2\Pi$	(5,115)	benzoato	48	20
	12,03,113	ູ້ເວີ ເວີ	2,3.Dichronopropyl acctate	1 %	97 97
	C.II.CO.Br	, IOO	2,3-Dibromopropyl butytato	١	97
	$c_{\rm eH_3}^{\rm L} co_{ m jBr}$		1.Chloro-2-butyl 3,5-dinitro-		90
	3,5.(NO <sub>2</sub> )2C <sub>6</sub> II <sub>3</sub> CO <sub>2</sub> C <sup>1</sup>	e corro	benzoato	1	2
	TE (NO.). C. H. CO. Br	CHCl3	1-Bromo-2-butyl 3,5-dinitro-	١	96
	7,0-(1,00,00,00,00,00,00,00,00,00,00,00,00,00		benzoato	١	96
	$3.5 \cdot (NO_2)_2 C_6 H_3 CO_2 I$	$(C_2H_5)_2O_3$	three-3-Iodo-2-butyl 3,5-dinitro-		ć
	$3,5\cdot(\mathrm{NO_2})_2\mathrm{C_6H_3CO_2I}$	(C2H5)2O	bonzoato	1	90
	$3,5.(\mathrm{NO_2})_2\mathrm{C_6H_3CO_2I}$	$(C_2H_5)_2O$	erythro-3-Iodo-2-butyl 3,5-dinitro-	١	96
	$3,5\cdot(\mathrm{NO}_2)_2\mathrm{C}_6\mathrm{H}_3\mathrm{CO}_2\mathrm{I}$	$(C_2H_5)_2O$	1-Iodo-2-mothyl-2-propyl 3.5-dinitrobenzoato	١	96

Butadieno	$C_{k}H_{s}CO_{s}I^{\dagger}$	$C_nH_n$	1,2,3,4-Butanototrol totrabenzoato	90	11
	$C_6^{\prime} H_5^{\prime} CO_2^{\prime} I_7^{+}$	$C_{f c}H_{f c}$	1-Butene-3,4-diol	80	11
			2-Butone-1,4-diol	4	
1-Pentene	$\mathrm{CH_3CO_2I}$	$C_{\mathbf{f}}\mathbf{H}_{\mathbf{f}}$	1,2-Pentanediol diacetate	Good	10
	C,H,CO,I	C,H,	1,2-Pentanediol dibenzoate	Good	10
	$3,5\cdot(\mathrm{NO_2})_2\mathrm{C_6H_3CO_2I}$	$(\ddot{\mathbf{C_2H_5}})_2\mathrm{O}$	1-Iodo-2-pentyl 3,5-dinitro-		
			benzoate	İ	96
Cyclopentene	$3,5\cdot(\mathrm{NO}_2)_2\mathrm{C}_6\mathrm{H}_3\mathrm{CO}_2\mathrm{I}$	$(C_2H_5)_2O$	2-Iodocyclopentyl 3,5-dinitro-		
			benzoate	İ	96
1-Hexene	$3,6$ - $(\mathrm{NO}_2)_2\mathrm{C_6H_3CO_2I}$	$(C_2H_5)_2O$	1-Iodo-2-hexyl 3,5-dinitro-		
			benzoate	1	96
Cyclohexene	$ m CH_3CO_2Br$	CCI⁴	2-Bromecyclohexyl acctato	35	22
	CH <sub>3</sub> CO <sub>2</sub> I§	$(C_2H_5)_2O$	2-Iodocyclohexyl acetate	80	21,94
	C2H5CO2Br	CHCl3; C6H6N	2-Bromocyclohexyl propionate	48	61 61
		$CHCl_3 + C_5H_5N$	2-Bromocyclohexyl n-butyrate	47	22
		CCI <sub>4</sub> 2-I	$2 ext{-Bromocyclohexyl} n ext{-butyrate} \ $	50	20
	(griscosofi 可以 (C) 用:C	CCI,	2-Chlorocyclohexyl benzoate	Good	14, 22
		CCI.	2-Bromocyclohexyl benzoate	40-45	20, 25
	C.H.CO.1		2-Bromocyclohexyl benzeate	Good	14
		(C2H5)2O; CCI4	$^{2 ext{-}\mathrm{Iodoeyclohexyl}}$ benzeate	09	14.21
		$C_{6}H_{6}$	(+, -)-trans-1,2-Cyclohexancdiol		
			dibenzeate	44	101

\* This reagent was used to identify olefins, 96 no yields were recorded though they are presumably high. A large excess of the complex and additional silver benzoate were employed.

New units at the complex was employed.

New units rather than silver accrate was used.

New different yourseless was itemed simultaneously.

101

2				OI	RGA:	SIC .	RE.	ACT	HC	NS	,							
Refer-	02110	61	101	101	96	9 9 9	95	95	10	10, 11	101	3	101	96	51	10	61	
3	Yıcld, %	77	72	10	1	80	50	09	-	1	ť		11	1	60	Good	09	
-Continued	Product	2-Bromocyclohexyl $m$ -nitro-benzoate	(+, -).trans-2-Bromocyclohexyl 3,5-dinitrobenzoato	(+, -).trans-1,2-Cyclohexanediol bis-3,5-dinitrobenzoate	2.Iodocyclohexyl 3,5-dinitro-	Di-2-jodoeyelohexyl carbonate	Di-2-iodocyclohexyl oxumeo	Di.2.iodoevelohexyl phthalato	1.9.5.6-Hexanetetrol tetrabenzoate	Syrup; mixture of diacetates	+,-).trans.t,5.Cyclohexenediol	dibenzoate	(1,4)R-1,2,4,5-Cyclohexanetetrol tetrabenzoate	1-Iodo-2-heptyl 3,5-dinitro-	Denzoulo	2.broino-1.phenyletny i accessed Phenylethanediol dibenzoato	(+).2.Bromo-1.phenylethyl 2.ethylhoxanoato	
TABLE XIII-Continued	Solvent	*IDD	$c_{ m eH_6}$	$\mathrm{C}_{\mathrm{c}}\mathrm{H}_{6}$	$(C_2H_5)_2O$	$(C_2H_5)_2O$	$(C_2H_5)_2O$	(C2H5)20	(Carra)20	Cene CH	CeH <sub>6</sub>	,	$C_{f G}H_{f G}$	$(C_2H_5)_2O$		cci,	CCI.	
•	Acyl Hypohalite	$^{,)}_{m ext{-} ext{NO}_2 ext{C}_6 ext{H}_4 ext{CO}_2 ext{Br}}$	$_{3,5\text{-}(\mathrm{NO}_2)_2\mathrm{C_6H_3CO}_2\mathrm{Br}}$		$_3,5$ -(NO $_2$ ) $_2$ C $_6$ H $_3$ CO $_2$ I	1.00	10,000I	${ m IO_2^CC(CH_2)_2CO_2I}$	$o$ - $\mathrm{C_6H_4(CO_2I)_2}$	C3H5CO2Br	CH,CO,I			$3,5.(\mathrm{NO}_2)_2\mathrm{C_6H_3CO_2I}$		CH <sub>3</sub> CO <sub>2</sub> Br	$\mathrm{c_6H_5^{CO_2^{11}}} (+)\mathrm{-c_4H_5^{0}CH(c_2^{2}H_5^{1})CO_2^{2}Br}$	
	Olefin	Cyclohexene (Contd.)								1,5-Hexadiene	2,4-Hexadiene	1,4-Cyclonexaglene		1.Heptene		Styrene		

rs of Acms	Reference	102	15	15	17	16	16	18	18	18
EN ON SILVER SAL	Yield, %	1	١	١	50	73-78	99	88	90	₹.
TABLE ALV	NUCLEAR HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION WITHOUT DECARBOXYLATION BY THE INCLEASE HALOGENATION BY THE INCLE	Preduct	3.BrC <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> H	3.1C <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> H	7.12.2.HOC6.112.CO2.11	2.Br.5.CH3OC6H3CO211	3-Br-4-CH3CC6113Cc211	3.br-4.CH <sub>3</sub> C <sub>6</sub> H <sub>3</sub> CC <sub>2</sub> tt 9. rs. f. CH. OC. H. (CH <sub>3</sub> ),CO.H	F'OD'(HD'CHTOCHTO:	$_{3.1.4.\mathrm{CH}_3\mathrm{OC}_6\mathrm{H}_3(\mathrm{CH}_2)_4\mathrm{CO}_2\mathrm{H}}$
	тои without L	Solvent	1	1	ł	, CC1,	CCI	CCI⁴	CCI <sup>‡</sup>	CCI
	NUCLEAR HALOGENAT	Acid	C,H,CO,H		$2.\mathrm{HOC_6H_4CO_2H}$	3.CH3.OC,H4.CO2.H	$_{4.\mathrm{CH_3OC_6H_4CO_2H}}$	$_4$ .CH $_3$ C $_6$ H $_4$ CO $_2$ H	$3\text{-CH}_3\text{OC}_6\text{H}_4\text{(CH}_2)_2\text{CO}_2\text{H}$	$_4$ -CH $_3$ OC $_6$ H $_4$ (CH $_2$ ) $_4$ CO $_2$ H

TABLE XV

NUCLEAR HALOGENATION OF AROMATIC SUBSTANCES BY THE ACTION OF SILVER ACETATE AND HALOGEN

Aromatic Substance	Solvent	Product	Yiold, %	Referenco
	CCI4	$4 \cdot \mathrm{BrC}_6\mathrm{H}_1\mathrm{OCH}_3$	50	17
L,CH,CO2H	$H_2OO_EHO$	$3.1.4.\mathrm{CH_3OC_6H_3CH_2CO_2H}$	88	18
3.CH3OC6H4(CH2)2CO2H	CH <sub>3</sub> CO <sub>2</sub> H	$2 \cdot Br \cdot 5 \cdot CH_3 OC_6 H_3 (CH_2)_2 CO_2 H$	eg S	18
	$CH_3CO_2H$	$2\text{-}1\text{-}5\text{-}\text{CH}_3\text{OC}_6\text{H}_3\text{(CH}_2\text{)}_2\text{CO}_2\text{H}$	84	18
$4.\mathrm{CH_3OC_6H_4(CH_2)_3CO_2H}$	$CH_3CO_2H$	$3.1.4.\mathrm{CH_3OC_6H_3(CH_2)_3CO_2H}$	98	18
$4\cdot \mathrm{C_2H_5OC_6H_4(CH_2)_3CO_2H}$	CH3CO2H	$3.1.4.C_2H_5OC_6H_3(CH_2)_3CO_2H$	80	18
$3,4\cdot(\mathrm{CH_3O})_2\mathrm{C_6H_3}(\mathrm{CH_2})_3\mathrm{CO}_2\mathrm{H}$	$\mathrm{CH_{3}CO_{2}H}$	$^{1\cdot1\cdot3,4(\mathrm{CH}_{3}\mathrm{O})_{2}\mathrm{C}_{6}\mathrm{H}_{2}(\mathrm{CH}_{2})_{3}\mathrm{CO}_{2}\mathrm{H}}$	81	18
$4\cdot\mathrm{CH_3OC_6H_4(CH_2)_4CO_2H}$	$CH_3CO_2H$	$3 \cdot 1 \cdot 4 \cdot \mathrm{CH}_3 \mathrm{OC}_6 \mathrm{H}_3 \mathrm{(CH}_2)_3 \mathrm{CO}_2 \mathrm{H}$	80	18
$4$ -CH $_3$ OC $_6$ H $_4$ (CH $_2$ ) $_5$ CO $_2$ H	CH3CO2H	$3.1.4.\mathrm{CH_3OC_6H_3(CH_2)_5CO_2H}$	5°F	18
$4 ext{-CH}_3\mathrm{OC}_6\mathrm{H}_4(\mathrm{CH}_2)_9\mathrm{CO}_2\mathrm{H}$	$CH_3CO_2H$	3-I-4-CH <sub>3</sub> OC <sub>6</sub> H <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> CO <sub>2</sub> H	26	18
$3.\mathrm{CH}_3.4.\mathrm{CH}_3\mathrm{OC}_6\mathrm{H}_3(\mathrm{CH}_2)_3\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5$	CH3CO2H	3-I-5 CH <sub>3</sub> -4-CH <sub>3</sub> OC <sub>6</sub> H <sub>2</sub> (CH <sub>2</sub> ),CO,C,H <sub>5</sub>	<b>7.</b>	18
$4\text{-CH}_3\mathrm{OC}_6\mathrm{H}_4(\mathrm{CH}_2)_5\mathrm{CO}_2\mathrm{C}_2\mathrm{H}_5$	CH3CO2H	3-I-4-CH <sub>3</sub> OC <sub>6</sub> H <sub>3</sub> (CH <sub>2</sub> ),CO,C,H,	88	· 8
$2,5 \cdot (\mathrm{CH_3})_2 \mathrm{C_6H_3} (\mathrm{CH_2})_9 \mathrm{CO_2C_2H_5}$	CH3CO2H		92	38
$^4\cdot\mathrm{CH_3OC_6H_4(CH_2)_9CO_2C_2H_5}$	CH3CO2H		76	S 2
$^4\cdot\mathrm{C_2H_5OC_6H_4}(\mathrm{CH_2})_9\mathrm{CO_2C_2H_5}$	$CH_3CO_2H$		78	S 2
$^{4\cdot C_{2}H_{5}OC_{6}H_{4}(CH_{2})_{10}CO_{2}C_{2}H_{5}}$	CH3CO2H		09	18

VI	
X	
3LE	
A.	

		TABLE XVI	TANA TO A CHOST AND	HALOGEN
(TANGOOLITE TITLE	TON OF AROMATIC	Reference Transmion of Aromatic Substances by the Action of Silver Vield % Reference	Vield. %	Reference
NUCLEAR HALOGENAL	Solvent	Produet	0/ (5)	19
Aromatic Substance	210100	C H.Br	33	10
C.H.	None	*1 11 5	85	61
99)	None	Centi	73	20
	22 23	$4 ext{-BrC}_6 ext{H}_4 ext{CH}_3$	06	19
$C_6 H_5 CH_3$	None	4-BrC,H,CH3	0	55
	LYON C	4.1C.H.CH,	ů.	10
			888	01
	None	4-1C6H4CH3	58	19
5 # 5	Nono	4-BrC <sub>6</sub> H <sub>4</sub> CiT	63	19
097790	None	4-IC <sub>6</sub> H <sub>1</sub> Ci†	109	10
ģ	Nono	$_4 ext{-BrC}_6 ext{H}_4 ext{Br}\dagger$	- F	19
C <sub>6</sub> rr <sub>5</sub> DI	None	$_{4 ext{-}1}$ C $_{6}$ H $_{4}$ Br	1 13	61
	Mono	4.BrC,H,I	66	9.0
$c_{\mathbf{f}}\mathbf{H_{\mathbf{f}}}\mathbf{I}$	OHOLI	- H C1 V	2.2	<u>.</u>
,	None	11VO 11 % ct .	76	61
C.H.OCH,	None	4-BrCentochia	10	19
0 0 0 0	None	4.1C <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub>	16 9	534
2 1 IOO 1 2 2	CHCI	4.Iodoveratrolo	90	0.0
$C_6H_4(OCH_3)_2^{-6}$	S	4. B.C. H.NH.	23	01
$C_kH_sNH_2$	None	17-V 11 C1 V	2]	61
	None	4-10 <sub>6</sub> 11 <sub>1</sub> 111 <sub>2</sub>	=	10
C.H.N(CH.)	None	4-1C <sub>6</sub> H <sub>3</sub> -\(\CH <sub>3</sub> \)2	01	10
2/5	Nono	$3 \cdot BrC_{\epsilon}H_{\epsilon}NO_{2}$	6-1	
Censino2	71	. SI EL	10	ß.
	Lyone	6 T CO II	61	10
C,H,CO,H	$C_6H_5NO_2$	J-DiCerricogram	1.2	19
1	C,H,NO,	3-1C <sub>6</sub> H <sub>3</sub> CO <sub>2</sub> H		92
9.Methylnanhthaleno	(C,H;),O	I.Bromo-2-methyinaphthaleno	00	2 5
Thiophene	None	2,5-Diiodothiophene	1	2
* Six per eent of diiodobenzene was also formed.	obenzene was also	formed.		

<sup>†</sup> The infrared absorption indicates the presence of ortho derivative. † The infrared absorption indicates the presence of ortho derivative. † Twenty-one per eent of CF<sub>3</sub>Br was also formed. § No 3-iodonitrobenzene was formed. ¶ The infrared absorption shows no ortho or para derivative.

TABLE XVII FORMATION OF HALOACETYLENES BY THE ACTION OF SILVER BENZOATE AND HALOGEN ON ACETYLENES

Acetylene	Acylhypohalite (or Simonini Complex)	Solvent	Product	Yield	Reference
HC≡CH	$(C_6H_5CO_2)_2AgI$	$C_6H_6$	HC≡CI		12
	$2(C_6H_5CO_2)_2AgI$	$C_6H_6$	IC=CI	<del></del>	12
$n \cdot C_5 H_{11} C = CH$	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> Cl	$CCl_4$	$C_5H_{11}C \equiv CCl$	Good	14
	$C_6H_5CO_2Br$	CCI <sub>4</sub>	$C_5H_{11}C \equiv CBr$	Good	14
	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> I	CCl4	$C_5H_{11}C \equiv CI$	Good	14
$C_6H_5C \equiv CH$	$(C_6H_5CO_2)_2AgI$	$C_6H_6$	$C_6H_5C \equiv CI$	Quant.	12

### CHAPTER 6

### THE SYNTHESIS OF $\beta$ -LACTAMS

# JOHN C. SHEEHAN Massachusetts Institute of Technology

#### AND

## ELIAS J. COREY University of Illinois

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### INTRODUCTION

The four-membered ring appears to be the smallest cyclic system that is capable of accommodating the amide function as a constituent. Such four-membered, cyclic amides (I), commonly referred to as  $\beta$ -lactams, possess physical and chemical properties that diverge sharply, partially



as a result of ring strain, from those of acyclic amides and lactams of greater ring size. Thus, in common with  $\beta$ -lactanes and cyclobutanone derivatives, the simple  $\beta$ -lactanes are unusually susceptible to reactions involving the carbonyl group and generally undergo facile ring cleavage. In addition, each of these small-ring systems presents considerable In addition, each of these small-ring systems presents considerable difficulty in synthesis. The reluctance with which  $\beta$ -lactanes are formed, difficulty in synthesis. The reluctance with which  $\beta$ -lactanes are formed, using the conventional methods of lactane synthesis, has necessitated using the conventional methods of lactanes are these compounds.

No authentic  $\beta$ -lactams were known until the beginning of the present century, probably because their synthesis by the method commonly used for  $\gamma$ -lactam formation, i.e. thermal dehydration of the appropriate amino acids, had not been realized. The first  $\beta$ -lactams were prepared amino acids, had not been realized. The first  $\beta$ -lactams were prepared by Staudinger and his co-workers, using two highly novel methods which were discovered in connection with their studies on the chemistry of ketenes. During the twenty-odd years between the completion of ketenes. During the twenty-odd years between the completion of ketenes, and 1943, two additional syntheses of  $\beta$ -lactams were discovered, and thereafter several more.

After 1943 interest in the synthesis and chemistry of  $\beta$ -lactams was stimulated by the importance of the natural penicillins and the problem of their structure and synthesis. When it became apparent that the of their structure and synthesis the  $\beta$ -lactam ring as a key feature, natural penicillins might possess the  $\beta$ -lactam ring as possibly related intensive studies were made of  $\beta$ -lactams, especially those possibly related

 $<sup>^1</sup>$   $\beta$ -Lactams may also be named as keto derivatives of the parent saturated heterocycle azetidine, i.e. as 2-azetidinones. This system of nomenclature has been used widely, cf. azetidine, i.e. as 2-azetidinones. This system of nomenclature has been used widely, cf. C.A., 38, 7061 (1944), and will be followed here in the naming of monocyclic  $\beta$ -lactams. C.A., 38, 7061 (1944), and will be followed here in the naming of monocyclic  $\beta$ -lactams. 2 Staudinger, Die Ketene, F. Enke, Stuttgart, 1912.

to the penicillins. Early evidence in favor of the now accepted  $\beta$ -lactamthiazolidine structure for the penicillins came from the investigation of the infrared absorption of the penicillins (II) and model  $\beta$ -lactams such as III.

After the  $\beta$ -lactam-thiazolidine formulation for the penicillins became generally accepted, it was realized that the known routes to  $\beta$ -lactams probably were inadequate for a practical synthesis of penicillin (II,  $R = C_6H_5CH_2$ ). This fact, coupled with the curious differences in the chemical properties (rate of formation, and reactivity toward certain reagents) of various  $\beta$ -lactams, has provoked continued research and interest in the field of the  $\beta$ -lactams.

Although there are at present several useful approaches to the  $\beta$ -lactam ring system, the synthesis of  $\beta$ -lactams by a single general method is not possible. Therefore, it is always necessary in problems of  $\beta$ -lactam synthesis to determine which of the available methods is best suited for the case at hand. In general, the preparation of  $\beta$ -lactams is more readily accomplished if the lactam being formed is highly substituted. These highly substituted  $\beta$ -lactams are usually more stable to ring-cleavage reactions than are the simpler  $\beta$ -lactams. The method of synthesis of these stable, easily formed  $\beta$ -lactams is commonly determined by the availability of the starting materials.

The problem of the synthesis of the less stable, highly reactive  $\beta$ -lactams, e.g. a penicillin, is much more difficult. Usually a number of the standard synthetic approaches to  $\beta$ -lactams are excluded at the outset because the necessary starting materials are unstable or cannot be prepared readily. Of the remaining methods, only those that involve mild reaction conditions, and hence highly reactive starting materials, present much likelihood of success. Thus, the outstanding problem in  $\beta$ -lactam synthesis is the development of new and efficient routes to the less stable  $\beta$ -lactams.

In principle, the synthesis of the  $\beta$ -lactam ring system might be accomplished by the formation of one, two, three, or all four bonds of the ring during the cyclization step. Of these four possibilities all but the last have been realized. All presently known routes to  $\beta$ -lactams in which only one bond is formed during cyclization involve formation of the amide linkage or the  $C_{\alpha}$  to  $C_{\beta}$  bond. The known syntheses of  $\beta$ -lactams that create two bonds all entail simultaneous formation of the same two bonds

i.e. carbonyl to nitrogen and  $C_{\alpha}$  to  $C_{\beta}$ . The only reported synthesis in which three bonds are established simultaneously involves formation of all but the amide bond, and it is this route, as might be expected, that is the least general.

#### CYCLIZATION OF β-AMINO ACID DERIVATIVES

As mentioned earlier, the thermal dehydration of  $\beta$ -amino acids to  $\beta$ -lactams has not as yet been achieved, partly because of the ease with which  $\beta$ -amino acids undergo  $\beta$ -elimination. However, a number of  $\beta$ -lactams have been formed from derivatives of  $\beta$ -amino acids. In particular, it is noteworthy that acyl derivatives of many  $\beta$ -amino acids are transformed into  $\beta$ -lactams in good yield by heating.<sup>3</sup> The reaction may be illustrated by the formation of 1-benzyl-3,3-dimethyl-4-phenyl-2-azetidinone (V) from the N-isobutyryl derivative IV in 50-60% yield.<sup>3</sup>

CCH<sub>3</sub>)<sub>2</sub>C—CO<sub>2</sub>H (CH<sub>3</sub>)<sub>2</sub>C—CO + (CH<sub>3</sub>)<sub>2</sub>CHCO<sub>2</sub>H 
$$C_6H_5$$
CH—NCOCH(CH<sub>3</sub>)<sub>2</sub>  $\rightarrow$   $C_6H_5$ CH—NCOCH(CH<sub>3</sub>)<sub>2</sub>  $\rightarrow$   $C_6H_5$ CH  $\rightarrow$   $C_6H_5$ 

This synthesis of  $\beta$ -lactams from  $\beta$ -acylamino acids was discovered by Staudinger<sup>3</sup> in connection with his studies of the reaction of ketenes with imines (which also leads to  $\beta$ -lactams). The ketene-imine reaction often affords piperidinediones, instead of, or in addition to,  $\beta$ -lactams, by the combination of one molecule of imine with two of the ketene, as shown below. In these cases the  $\beta$ -lactam can frequently be prepared indirectly.

below. In these cases the 
$$\beta$$
-lactam can frequently be prepared indicately  $R_2''C-C=O$   $R_2''C+C=O$   $R_2''C+C=O$   $R_2''C-C=O$   $R_2''C-C=O$   $R_2''C-C=O$   $R_2''C-C=O$   $R_2''C-C=O$   $R_2''C-C=O$   $R_2''C-C=O$  Hydrolynia  $S$  (1) a simulatinadianes proceeds readily and yields the

Hydrolysis of the piperidinediones proceeds readily and yields the  $\beta$ -acylamino acids, which can subsequently be cyclized to  $\beta$ -lactams. This three-step method is applicable not only to the preparation of monocyclic  $\beta$ -lactams but also to certain fused  $\beta$ -lactam-thiazolidines such as VI.4

Staudinger, Klever, and Kober, Ann., 374, 1 (1910).
 Clarke, Johnson, and Robinson, The Chemistry of Penicillin, Princeton University Press, 1949

The relatively facile formation of  $\beta$ -lactams by this route may be due to the possibility of closing the  $\beta$ -lactam ring by O to N acyl rearrangement of an intermediate hydroxylactone, such as VII, in the formation of IV. Such a reaction path would explain the function of the acyl group in promoting cyclization.

The cyclization of  $\beta$ -amino acids through the use of reagents such as acetyl chloride, phosphorus trichloride, and thionyl chloride has been accomplished in a limited number of cases. Thus  $\beta$ -benzylamino- $\beta$ -phenyl- $\alpha$ , $\alpha$ -dimethylpropionic acid (VIII)<sup>3</sup> and  $\beta$ -phenyl- $\beta$ -anilino-propionic acid (IX)<sup>5</sup> have been transformed into the corresponding  $\beta$ -lactams by treatment with acetyl chloride and phosphorus trichloride, respectively.

$$\begin{array}{cccc} \mathbf{C_6H_5CHC(CH_3)_2CO_2H} & & \mathbf{C_6H_5CHCH_2CO_2H} \\ & & & & & \\ & & \mathbf{NHCH_2C_6H_5} & & & \mathbf{NHC_6H_5} \\ & & & & \mathbf{IX} \\ \end{array}$$

An example of a cyclization of the above type is the synthesis of a phthaloylpenicillin (XI) from the corresponding phthaloylpenicilloic acid (X) in 12% yield by means of thionyl chloride.<sup>6</sup> It is interesting also to note

that benzylpenicilloic acid (XII) has been converted in trace yield to benzylpenicillin (XIII)<sup>7</sup> using phosphorus trichloride.

Another variant of the route to  $\beta$ -lactams via  $\beta$ -amino acid derivatives is due to Breckpot.<sup>8</sup> This synthesis, which involves the base-catalyzed cyclization of a  $\beta$ -amino acid ester using a Grignard reagent as the base, is illustrated by the synthesis of 1-ethyl-4-methyl-2-azetidinone (XIV).

<sup>&</sup>lt;sup>5</sup> Ref. 4, p. 975.

<sup>&</sup>lt;sup>6</sup> Sheehan, Henery-Logan, and Johnson, J. Am. Chem. Soc., 75, 3292 (1953).

<sup>7</sup> Süs, Ann., 571, 201 (1951).

<sup>&</sup>lt;sup>8</sup> Breckpot, Bull soc. chim. Belg., 32, 412 (1923).

The method is especially advantageous if there are only one or two substituents on the  $\beta$ -lactam ring being formed, or if the substituents are alkyl groups.

$$\begin{array}{c} \operatorname{CH_3CH-CH_2CO_2C_2H_5} & \xrightarrow{C_2\Pi_5\operatorname{MgBr}} & \operatorname{H_3CCH-CH_2} \\ \mid & \mid & \mid \\ \operatorname{C_2H_5NH} & \xrightarrow{40^o_{\bullet}} & \operatorname{H_5C_2N-CO} \end{array}$$

A large number of monocyclie  $\beta$ -lactams,  $^{8-11}$  including 2-azetidinone itself,  $^{11}$  have been synthesized by this method. The yields of  $\beta$ -lactam decrease markedly as the number of substituents on the  $\beta$ -lactam ring being formed decreases, but the method is frequently operable in instances where others fail. The yields obtained for a series of  $\beta$ -lactams possessing two, one, or no substituents are indicated below.

### Experimental Procedures

3,3-Dimethyl-1-ethyl-4-phenyl-2-azetidinone (Cyclization of a β-Acylamino Acid).<sup>4</sup> (a) 1-Ethyl-6-phenyl-3,3,5,5-letramethyl-2,4-piper-idinedione. To 5.6 g. of N-benzylidencëthylamine (prepared from benzal-dehyde and ethylamine) in an atmosphere of nitrogen is added a solution of 5.9 g. of dimethylketene<sup>12</sup> in 60 ml. of ethyl acetate. The solution becomes colorless after about six hours and is stored at room temperature for an additional fourteen hours. The ethyl acetate is removed under reduced pressure, leaving a crystalline residue weighing 8,08 μ. Recrystallization, from benzene-petroleum ether gives a 43% yield of colorless crystals of the piperidinedione, m.p. 89-90°.

honr (until bubbling stops). During this time 1.9 g. of isobutyric acid is collected. The pressure is reduced, and the product is distilled at 92-100°/2 mm., yielding 3.8 g. (87%) of the azetidinone.

1,4-Diphenyl-2-azetidinone (Cyclization of a  $\beta$ -Amino Acid).<sup>4</sup> A mixture of 1.2 g. of  $\beta$ -anilino- $\beta$ -phenylpropionie acid and 2.4 ml. of phosphorus triehloride is refluxed for one-half hour. The reagent is then removed as completely as possible under reduced pressure, and the gummy residue is triturated with two 15-ml. portions of water and crystallized from cold methanol. The yield of  $\beta$ -lactam, m.p.  $154-155^{\circ}$ , is 0.6 g. (53%).

1-Benzyl-4-phenyl-2-azetidinone (Cyclization of a  $\beta$ -Amino Acid Ester). To a solution of 8.01 g. of ethyl  $\beta$ -benzylaminohydroeinnamate in 70 ml. of dry ether is added 14 ml. of a 2N solution of ethylmagnesium bromide in ether as rapidly as the evolution of gases permits. The mixture that results is allowed to stand at room temperature for ninety minutes and is then decomposed by cautious addition of an excess of 10% aqueous ammonium ethoride. The mixture is agitated until all the solid dissolves, and the ethereal solution is separated and washed with two small portions of water. The aqueous washes are extracted with ether, and the ethereal solutions are combined, dried, and evaporated to constant weight.

The neutralization equivalent of the residual oil is determined by titration with standard hydrochloric acid. From the neutralization equivalent, the amount of standard (ca. 4N) ethanolic hydrogen chloride required to neutralize the free amino groups is added to the oil. Most of the ethanol is removed by evaporation under reduced pressure. The residue is triturated with 25 ml. of ether, and the ethereal solution is separated from the hydrochloride by filtration. The filtrate is evaporated, and the residue is extracted with boiling ligroin. The ligroin is evaporated from the extracts, and the liquid remaining is distilled. The yield of slightly yellow 1-benzyl-4-phenyl-2-azetidinone, b.p. 145–150°/2 mm., is 3.0 g. (45%).

### REACTION OF IMINES WITH $\alpha\text{-}BROMOESTERS$ AND ZINC

In 1943 it was discovered that the reaction of benzylideneaniline with ethyl bromoacetate and zinc produces a  $\beta$ -lactam, 1,4-diphenyl-2-azetidinone (XV), in 56% yield.<sup>13</sup> Little work has been done to determine

<sup>13</sup> Gilman and Specter, J. Am. Chem. Soc., 65, 2255 (1943).

the scope of this synthesis although a number of  $\beta$ -lactams have been prepared by this method in yields as high as 85%.4,13 There is a strong resemblance between this reaction and that discovered by Breekpot in that both probably proceed by nucleophilic attack of an intermediate amide ion on the carbalkoxyl function with displacement of alkoxide ion and simultaneous closure of the  $\beta$ -lactam ring.

### Experimental Procedure

1,4-Diphenyl-2-azetidinone.13 A solution of 36.2 g. of benzylideneaniline in 200 ml. of dry toluene is heated to boiling with 13.5 g. of sandpapered zinc foil and a crystal of iodine. Three milliliters of ethyl bromoacetate is added, and on stirring an exothermic reaction sets in. An additional 20 ml. of the bromoester is added at a rate such as to maintain gentle refluxing. When the addition is complete, the mixture is heated to reflux for one-half hour. The reaction mixture is hydrolyzed with 200 ml. of concentrated ammonium hydroxide, and the toluene layer is separated, washed successively with water, dilute hydrochloric acid, sodium bisulfite solution, and water, and finally evaporated to dryness. Two recrystallizations of the residue from methanol afford the β-lactam, m.p. 153-154°, in 56% yield.

### DIRECT COMBINATION OF KETENES WITH IMINES

The reaction of ketenes, in particular disubstituted or "ketoketenes," with imines provides a good route to some types of substituted monoand bi-cyclic  $\beta$ -lactams. Diphenylketene, for example, reacts readily with benzylideneaniline at room temperature to yield the crystalline β-lactam, 1,3,3,4-tetraphenyl-2-azetidinone (XVI) in 72% yield. 14 This was the first known  $\beta$ -lactam. 15 Most of the  $\beta$ -lactams prepared by

this method have been made from dimethyl-2,16,17 or diphenyl-ketene,2,14,18 which seem in general to react smoothly with Schiff bases derived from

<sup>&</sup>lt;sup>15</sup> None of the substances that had been previously reported as  $\beta$ -lactams in the literature really appears to possess the  $\beta$ -lactam structure. These cases are discussed in ref. 4, pp. 982-984.

<sup>16</sup> Staudinger and Klever, Ber., 40, 1149 (1907).

<sup>&</sup>lt;sup>17</sup> Holley and Holley, J. Am. Chem. Soc., 73, 3172 (1951).

<sup>18</sup> Staudinger and Jelagin, Ber., 44, 365 (1911).

aromatic aldehydes or ketones and aromatic amines. Other ketenes which have been used in this synthesis include diethylketene,19 ethylearbethoxyphenylearbomethoxyketene,<sup>20</sup> methylphenylketene,<sup>2</sup>  $ketene.^{2,20}$ biphenyleneketene,2 and ketene itself.20 The order of reactivity for several of these ketenes toward benzophenoneanil has been determined by Staudinger to be as shown below. This order of reactivity parallels

$$C=C=O>(C_{6}H_{5})_{2}C=C=O>C_{6}H_{5}(CH_{3})C=C=O\cong(CH_{3})_{2}C=C=O$$

that observed by Staudinger in the reaction of ketenes with benzyl alcohol.2 Ketene itself is much less reactive than the substituted ketenes which have been studied, for the coupling of ketene with benzylideneaniline takes place only at temperatures near 200°.20

The successful use of monosubstituted ketenes, "aldoketenes," in the synthesis of  $\beta$ -lactams has yet to be reported. This is not surprising because monosubstituted ketenes react with imines extremely slowly and even under mild conditions show a great tendency to polymerize.2

The scope of the ketene-imine method for making  $\beta$ -lactams is limited drastically by the types and number of imines that can react to form the desired products. All but one of the  $\beta$ -lactams which have been prepared by this method have been obtained from imines in which both the earbon and the nitrogen atom of the imino linkage are substituted by aromatic groups. No systematic study has been made of the effect of varying the substituents on the aromatic groups, although Staudinger has found that the reactivity of benzylidene-p-nitroaniline with diphenylketene is slight eompared to that of benzylideneaniline. A p-dimethylamino substituent, on the other hand, appears to increase the reactivity of aromatic Schiff bases. Perhaps it is also significant that acetophenoneanil is much less reactive to diphenylketene than is benzylideneaniline, although benzophenoneanil is much more reactive.2

Several other types of compounds containing the imino group, as for example the imido chloride XVII, the phenylhydrazone XVIII, and the oxime-ether XIX were found to be unreactive.2,14

<sup>20</sup> Staudinger, Ber., 50, 1035 (1917).

<sup>19</sup> Staudinger and Maier, Ann., 401, 292 (1913).

The presence of a sulfur substituent on the carbon of the imino grouping does not prevent  $\beta$ -lactam formation. The imido thioester XX reacts readily with dimethylketene to give the  $\beta$ -lactam XXI in 60% yield.<sup>17</sup>

In a single instance a fused  $\beta$ -lactam-thiazolidine (XXII) has been prepared from 2-phenyl-2-thiazoline and diphenylketene. This  $\beta$ -lactam served as a key model compound in the infrared studies on the structure of

$$(C_{6}H_{5})_{2}C = C = O + H_{5}C_{6}C CH_{2} \rightarrow (C_{6}H_{5})_{2}C = C CH_{2}$$

$$N = CH_{2}$$

$$XXII$$

penicillin.22 Substitution of dimethylketene for diphenylketene in the reaction with 2-phenyl-2-thiazoline does not result in formation of a β-lactam but, as mentioned previously, a piperidinedione.

Although considerable study<sup>4</sup> has been made of the preparation of fused  $\beta$ -lactam-thiazolidines closely related to penicillin by the combination of ketenes with suitable thiazolines [e.g., 2-thiazoline (XXIII) and methyl 5,5-dimethyl-2-thiazoline-4-earboxylate (XXIV)], no sneecssful results have been reported.

There are two cases in which the reaction of ketenes with imines is of special interest. The first is the combination of diphenylketene with cinnamylideneaniline which has been shown to lead to the  $\beta$ -lactam XXV instead of the  $\delta$ -lactam XXVI to be expected from 1,4 addition. 14,23

<sup>&</sup>lt;sup>21</sup> Ref. 4, p. 996.

<sup>&</sup>lt;sup>22</sup> Ref. 4, p. 405.

n Penicillin Program Report, Shell 14, 215.

The occurrence of 1,2 instead of 1,4-addition strikingly demonstrates the increased ease of formation of highly substituted  $\beta$ -lactams.

The reaction of ethylearbethoxyketene (XXVII) with benzylideneaniline occurs readily at  $-10^{\circ}$  to give a crystalline 1: 1 adduct which is not the  $\beta$ -lactam XXVIII and which was formulated by Staudinger as XXIX. The adduct is unstable and decomposes slowly at room temperature into the original imine and ketene. Upon heating this compound

at 170° the isomerie  $\beta$ -lactam XXVIII is formed. The  $\beta$ -lactam can also be obtained directly from the ketene and the imine at 180°. At present there is no eogent evidence in favor of structure XXIX for the unstable adduct, and structure XXX must be regarded as being at least equally possible.

$$C_2H_5OC \longrightarrow CC_2H_5$$
 $O$ 
 $CO$ 
 $H_5C_6CH \longrightarrow NC_6H_5$ 
 $XXX$ 

Phenylcarbomethoxyketene (XXXI) which might be expected to be more reactive to 1,2-addition than ethylcarbethoxyketene yields a  $\beta$ -lactam directly with benzylideneaniline. No intermediate product has been isolated. Dicarbethoxyketene (XXXII), on the other hand, does not appear to afford a  $\beta$ -lactam with benzylideneaniline under any conditions,

Several unsuccessful attempts have been made to form  $\beta$ -lactams by the combination of imines with the rearrangement products, presumably

ketenes, of diazo ketones. The reaction of phenylacetylcarbamyldiazomethane (XXXIII) with methyl 5,5-dimethyl-2-thiazoline-4-carboxylate in the presence of silver oxide, which might have afforded methyl benzylpenicillinate, produced a complex mixture which had little or no bioactivity.24

### Experimental Procedure

 $2,\alpha,\alpha$ -Triphenyl-2-thiazolidineacetic Acid  $\beta$ -Lactam.<sup>4</sup> Three and nine-tenths grams of diphenylketene<sup>25</sup> is added to 3.3 g. of 2-phenyl-2thiazoline.26 After five minutes the spontaneous heating ceases, and the mixture is warmed to 60-70° for five minutes. The product is taken up in warm toluene, diluted with low-boiling petroleum ether and cooled to give 4.5 g. of the  $\beta$ -lactam (63% yield) as a colorless solid, m.p. 140–143°.

### REACTION OF KETENES WITH NITROSO COMPOUNDS

During the course of an investigation of the reaction of ketenes with nitroso compounds, Staudinger and Jelagin<sup>18</sup> found that equimolar amounts of diphenylketene and nitrosobenzene gave a 63-65% yield of a product assigned structure XXXIV, and that a 2:1 molar ratio of the ketene and nitroso compound gave a mixture of products consisting mainly of XXXIV together with a small amount of the β-lactam XXXV.18 It Was suggested that the  $\beta$ -lactam is formed by addition of diphenylketone to benzophenoneanil which is produced by the decarboxylation of the

copnenoneanil which is produced by 
$$(C_6H_5)_2C-CO$$
  $(C_6H_5)_2C-CO$   $(C_$ 

intermediate XXXVI. p-Dimethylaminonitrosobenzene, which found to be more reactive than nitrosobenzene, afforded a 65% yield of the 21 the  $\beta$ -lactam when treated with two moles of diphenylketene and yielded no product corresponding to XXXIV. Nitroso derivatives of secondary amines such as diphenylamine and diethylamine do not react with diphenylketene to give  $\beta$ -lactams. 18

### REACTION OF AN IMINE, AN ACID CHLORIDE, AND A TERTIARY AMINE

One of the most recent syntheses of  $\beta$ -lactams, developed in connection with the problem of penicillin synthesis, involves the combination of an imine or thiazoline and an acid chloride, with loss of hydrogen chloride,

<sup>&</sup>lt;sup>24</sup> Ref. 4, p. 990.

<sup>25</sup> Org. Syntheses, 20, 47 (1940).

<sup>&</sup>lt;sup>24</sup> Wenker, J. Am. Chem. Soc., 57, 1079 (1935).

in the presence of a tertiary amine.27,28 An example of this synthesis is the reaction of benzylideneaniline with phthaloylglycyl chloride in the presence of triethylamine to give 1,4-diphenyl-3-phthalimido-2-azetidinonc (XXXVII) in 50% yield.27 The reaction proceeds rapidly at room temperature in inert solvents. By hydrazinolysis of the phthaloyl group

$$\begin{array}{c} \text{XCH}_2\text{COCl} + \text{C}_6\text{H}_5\text{CH} = \text{NC}_6\text{H}_5 \\ + (\text{C}_2\text{H}_5)_3\text{N} \end{array} \xrightarrow{\begin{array}{c} \text{C}_6\text{H}_6 \\ \text{XXYVII} \end{array}} \begin{array}{c} \text{H}_5\text{C}_6\text{CH} - \text{NC}_6\text{H}_5 \\ \text{I} \\ \text{XCH} - \text{CO} \\ \text{XXXVII} \end{array} \xrightarrow{+ (\text{C}_2\text{H}_5)_3\text{NHCl}}$$

X = Phthalimido

the phthalimido  $\beta$ -lactam XXXVII can be converted to an amino  $\beta$ -lactam and thence to other acylamino derivatives.<sup>27</sup>

Thiazolines bearing a 2-aryl or 2-carbalkoxy substituent also yield β-lactams in this reaction. Thus, 2-phenyl-,28 2-p-nitrophenyl-,29 and 2-furyl-thiazolines30 react with phthaloylglycyl chloride and triethylamine to give good yields of the corresponding  $\beta$ -lactams.

The synthesis of a 5-phenylpenicillin (XXXIX) has been carried out by this approach, using methyl 2-phenyl-5,5-dimethyl-2-thiazoline-4-carboxylate (XXXVIII) and succinylglycyl chloride as indicated below. 31,32

$$\begin{array}{c} \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{CC}_{6}\text{H}_{3} \\ \text{CC}_{6}\text{CC}_{6}\text{H}_{3} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{CC}_{6}\text{H}_{5} \\ \text{CC}_{6}\text{CC}_{6}\text{CC}_{6}\text{H}_{3} \\ \text{CC}_{6}\text{CC}$$

<sup>32</sup> Sheehan and Laubach, J. Am. Chem. Soc., 73, 4376 (1951).

<sup>&</sup>lt;sup>27</sup> Shechan and Ryan, J. Am. Chem. Soc., 73, 1204 (1951).

<sup>28</sup> Shechan and Ryan, J. Am. Chem. Soc., 73, 4367 (1951).

<sup>&</sup>lt;sup>29</sup> J. C. Shechan and K. Henery-Logan, unpublished results.

<sup>&</sup>lt;sup>20</sup> E. J. Corey, Ph.D. Thesis, Massachusetts Institute of Technology, 1951; J. A. Erickson, Ph.D. Thesis, Massachusetts Institute of Technology, 1953.

<sup>31</sup> Sheehan, Buhle, Corey, Laubach, and Ryan, J. Am. Chem. Soc., 72, 3828 (1950).

The acid chloride-thiazoline reaction is apparently very sensitive to the nature of the ring substituents. No lactam was isolated with thiazolines possessing a hydrogen, sulfhydryl, or chlorine substituent in the 2-position.<sup>33</sup> In addition, the reaction proceeds better with 2-phenyl-2-thiazoline than with methyl 2-phenyl-5,5-dimethyl-2-thiazoline-4carboxylate, while ethyl 2-phenyl-2-thiazoline-4-carboxylate is intermediate in behavior. Thus, the yields of  $\beta$ -lactam obtained with these three thiazolines are 50%,28 20%,34 and 34%35 respectively.

To date the acid chloride-imine synthesis has been applied only to the synthesis of acylamino  $\beta$ -lactams. The acid chlorides that have been used successfully in the reaction include phthaloyl- and succinyl-glycyl chloride, 5-phenyl-2,4-diketo-3-oxazolidineacetyl chloride<sup>36</sup> (XL), and 2-benzylidene-4,5-diketo-3-oxazolidineacetyl chloride<sup>37</sup> (XLI). The last two substances were employed because the heterocyclic systems which they contain can be degraded, once the  $\beta$ -lactam ring has been formed, to the phenylacetylamido substituent which is characteristic of benzylpenicillin (II,  $R = C_6H_5CH_2$ ). These degradations are indicated by the

accompanying formulas. 
$$^{36,37}$$
 $C_6H_5CH$ 
 $C_6H_5$ 
 $O-C$ 
 $OC-CO$ 
 It is important to note that acylamino acid chlorides of the type XLII are not generally available for use in the acid chloride-thiazoline synthesis

<sup>33</sup> J. C. Sheehan and co-workers, unpublished observations.

<sup>34</sup> Shechan, Hill, Jr., and Buhle, J. Am. Chem. Soc., 73, 4373 (1951). D. A. Johnson, Ph.D. Thesis, Massachusetts Institute of Technology, 1952.
 Ch. A. Johnson, Ph.D. Thesis, Massachusetts Institute of Technology, 1952.

<sup>&</sup>lt;sup>37</sup> Sheehan and Corey, J. Am. Chem. Soc., 73, 4756 (1951).

since attempts to obtain them from the corresponding acids usually lead to formation of salts of azlactones (XLIII). Thus, it is necessary to employ systems in which the nitrogen atom is protected from azlactonization by the presence of a suitable blocking group.

Benzencsulfonylglyeyl ehloride (XLIV) and carbobenzoxyglycyl ehloride (XLV), which cannot azlactonize but which possess an unprotected nitrogen atom, react with benzylideneaniline to form 4-imidazolones in yields of about 75%.38

$$\begin{array}{c} \text{RNHCH}_2\text{COCl} + \left| \begin{array}{c} \text{CHC}_6\text{H}_5 \\ \text{N} \end{array} \right| \\ \text{NC}_6\text{H}_5 \\ \text{NLIV} \quad \text{R} = \text{C}_6\text{H}_5\text{SO}_2 \\ \text{NLV} \quad \text{R} = \text{C}_6\text{H}_5\text{CH2}\text{COCO} \end{array}$$

Although it is clear at present that the acid chloride-imine (or thiazoline) reaction is by no means general for acid chlorides or imines, the exact scope of the reaction is still unknown. In addition, nothing is known about the mechanism of the reaction. Under some conditions there have been isolated crystalline by-products which have been tentatively formulated as acyl derivatives of enolized piperidinediones on the basis of elemental and infrared analysis. 25,31 The formation of such by-products can usually be minimized by working at very high dilution and operating with refluxing chloroform rather than methylene chloride as the solvent 25,20,31

2-Phenyl- $\alpha$ -succinimido-2-thiazolidineacetic Acid  $\beta$ -Lactam.  $^{32}$ To a solution of 1.63 g. of 2-phenyl-2-thiazoline26 in 10 ml. of methylene chloride (dried over Drierite) in a 200-ml. three-necked flask is added 1.85 g. of succinylglycyl chloride in 25 ml. of methylene chloride. To this rapidly stirred solution at reflux is added through a high-dilution cycle<sup>39</sup> a solution of 1.02 g. of triethylamine in 50 ml. of methylene chloride over a six-hour period. The resulting amber solution is concentrated under reduced pressure to a brown magma, which is shaken with 50 ml. of benzene. The colorless, crystalline residue of triethylammonium chloride (1.50 g., ca. 100%) is removed by filtration, and the filtrate is concentrated to a brown oil which partially crystallizes on standing for several days. The mixture is triturated with 20 ml. of 50% aqueous ethanol, allowed to stand overnight, and filtered. The crude lactam, crisp yellow needles, m.p. 148-160°, weighing 1.70 g., is purified by recrystallization from dioxane-water (Norit). The yield of essentially pure lactam, m.p. 166-168°, is 0.9 g. (30%).

# DEHYDROHALOGENATION OF N-α-HALOACYLAMINOMALONIC

Another reaction sequence by which a  $\beta$ -lactam can be formed is the establishment of an amide linkage by chloroacetylation of a substituted aminomalonic ester and subsequent base-catalyzed ring closure by the formation of a carbon-carbon bond. A specific example is furnished by the preparation of 1-phenyl-4,4-dicarbethoxy-2-azetidinone (XLVI) from anilinomalonic ester.40

The reaction appears to be general for N-substituted aminomalonic esters N-acylated with \alpha-haloacids, and the yields obtained are invariably high 40 41 high. 40,41 No dimeric or linear condensation products have been observed.

The analysis of the state of the The exact nature of the basic reagent is not important since tricthylamine, diethylamine, benzylamine, alcoholic ammonia, and alcoholic potassium

<sup>&</sup>lt;sup>29</sup> Cope and Herrick, J. Am. Chem. Soc., 72, 983 (1950).

<sup>&</sup>lt;sup>40</sup> Sheehan and Bose, J. Am. Chem. Soc., 72, 5158 (1950). 1 Sheehan and Bose, J. Am. Chem. Soc., 73, 1761 (1951).

hydroxide all have been used successfully in the ring-closure.<sup>41</sup> The  $\beta$ -lactams obtained by this process can be converted to  $\beta$ -lactams bearing a single carbethoxyl substituent, e.g. XLVII, by selective hydrolysis of one ester function and decarboxylation of the resulting acid.

This method of synthesis, although efficient, is obviously restricted to the preparation of  $\beta$ -lactams which possess one or two carboxyl (or similar) functions at the 4-position. A further limitation results from the fact that N-unsubstituted N-haloacylaminomalonic esters containing a hydrogen atom attached to the nitrogen atom, such as XLVIII, apparently do not undergo cyclization upon treatment with tertiary amines or other bases.<sup>41</sup>

 $\begin{array}{c} {\rm CICH_2CONHCH(CO_2C_2H_5)_2} \\ {\rm xLVIII} \end{array}$ 

#### Experimental Procedure

1-Phenyl-3-ethyl-4,4-dicarbethoxy-2-azetidinone.<sup>41</sup> A solution of 2 g. of  $\alpha$ -bromo-n-butyric acid, 1 ml. of phosphorus trichloride, and 2 g. of diethyl anilinomalonate<sup>42</sup> in 50 ml. of benzene is heated under reflux for two hours. After removal of the solvent, the residue is taken up in ether and washed with 5% aqueous sodium carbonate. Evaporation of the ether affords 2.84 g. of crude diethyl N-( $\alpha$ -bromo-n-butyryl)-anilinomalonate as a viscous oil. A benzene solution of this crude material containing 2 g. of triethylamine is heated to 50–60° overnight. After removal of the insoluble triethylammonium chloride and solvent and evaporative distillation of the residue at  $130-145^{\circ}/0.4$  mm., 2.29 g. (78% yield based on the malonic ester) of  $\beta$ -lactam is obtained as a colorless, viscous liquid,  $n_D^{25}$  1.5108.

#### MISCELLANEOUS SYNTHESES

An unusual approach to the  $\beta$ -lactam ring system is provided by the reaction of diazomethane with isocyanates. Diazomethane and phenyl isocyanate combine, in a manner reminiscent of the formation of cyclobutanone from ketene and diazomethane, to form 1-phenyl-2-azetidinone. <sup>43</sup> p-Bromophenylisocyanate is also converted to a  $\beta$ -lactam under these conditions. The reaction does not appear to be general, however, since no  $\beta$ -lactam could be isolated from the reaction of diazomethane with either  $\alpha$ -naphthyl-, p-nitrophenyl-, benzyl-, or benzoyl-isocyanate.

Several  $\beta$ -lactams have been prepared by modification of the substituents present in preformed  $\beta$ -lactam systems. Examples were mentioned in

<sup>42</sup> Blank, Ber., 31, 1812 (1898).

<sup>43</sup> Sheehan and Izzo, J. Am. Chem. Soc., 70, 1985 (1948); 71, 4059 (1949).

the preceding sections. Perhaps the best-known example of such a eonversion, however, is the synthesis of methyl desthiobenzylpenicillinate (XLIX) by desulfurization of methyl benzylpenicillinate with Raney nickel.<sup>4</sup>

Oxidation of fused  $\beta$ -lactam-thiazolidines produces, in general, the corresponding  $\beta$ -lactam-thiazolidine-1,1-dioxides in good yield.<sup>4</sup>

Finally, a number of  $\beta$ -laetams substituted by cyclohexyl groups have been prepared by catalytic reduction of the corresponding phenyl-substituted  $\beta$ -laetams.<sup>4</sup>

### TABULAR SURVEY OF SYNTHESES OF β-LACTAMS

An attempt has been made to collect in the following tables all examples of  $\beta$ -lactam syntheses that have been published before 1953. A few syntheses published subsequently are also included. Table I includes monocyclic  $\beta$ -lactams, and Table II the fused  $\beta$ -lactam thiazolidines. The sections of each table are arranged in a sequence determined by the number of substituents on the  $\beta$ -lactam ring. The following abbreviations are used for preparative methods: A, cyclization of  $\beta$ -amino acid esters with organometallic compounds; B, cyclization of  $\beta$ -acylamino acids; C, from  $\beta$ -amino acids; D, from imines,  $\alpha$ -bromoesters, and zinc; E, from ketenes and imines; E, from ketenes and nitroso compounds; E, from acid chlorides, imines, and tertiary amines; E, dehydrohalogenation of E-a-haloacylaminomalonic esters; E, from isocyanates and diazomethane; E, from a preformed E-lactam.

#### TABLE I—Continued

### MONOCYCLIC β-LACTAMS—AZETIDINONES



$\beta$ -Lactam (Substituents on Azetidinone Ring)	Yield, %	Method Preparat	of Refer-
TrisubstitutedContin	nued		
1,4-Diphenyl-3-amino (hydrochloride) 1,4-Diphenyl-3-phenylacetamido 1,4-Diphenyl-3-(2'-benzylidene-4',5'-diketo- 3'-oxazolidyl) 1,4-Diphenyl-3-(3'-nitrophthalimido) 1,4-Diphenyl-3-dimethanesulfonamido 1,4-Diphenyl-3-methanesulfonamido	54 56 17 16 54 39	J J G G G J	27 27 37 37 27 38 38
Tetrasubstituted			
1,3,3-Trimethyl-4-phenyl 1-Benzyl-3,3-dimethyl-4-phenyl  1,4-Diphenyl-3,3-dimethyl 1,4-Diphenyl-3,3-diethyl 1,4-Diphenyl-3-ethyl-3-carbethoxy 1,3,4-Triphenyl-3-carbomethoxy 1,3,3-Triphenyl-4-styryl 1-Phenyl-3,3-dimethyl-4-p-dimethylaminophenyl 1-Benzhydryl-3,3-dimethyl-4-phenyl 1-Phenyl-3,3-dimethyl-4-styryl 1-Phenyl-3,3-dimethyl-4-styryl	65 10 70 50–60 82 1 72 70	$egin{array}{c} B & E & C & B & E & E & E & E & E & E & E & E & E$	3, 4 3 4 3 16 19 20 20 16 14 2 2
1-p-Nitrophenyl-3,3-dimethyl-4-phenyl 1-Ethyl-3,3-dimethyl-4-phenyl 1,3,4-Triphenyl-3-methyl 1-Phenyl-3-methyl-4,4-dicarbobenzoxy 1-Phenyl-3-ethyl-4,4-dicarbothoxy  Pentasubstituted	87 ————————————————————————————————————	E B B H H	2 4 44 41 41
	84	E	
Pentaphenyl  1-p-Dimethylaminophenyl-3,3,4,4-tetraphenyl  1,4,4-Triphenyl-3,3-dimethyl 1,4-Diphenyl-3,3,4-trimethyl 1,3,4,4-Tetraphenyl-3-methyl 1,4,4-Triphenyl-3,3-o-biphenylene 1,4-Diphenyl-3,3-dimethyl-4-methylmereapto	100 65 — — — — 60	E F E F E E E E E	18 18 18 18 2 2 2 2 2 17
44 Staudinger and Ruzicka, Ann., 380, 301 (1911).			

### CHAPTER 7

### THE PSCHORR SYNTHESIS AND RELATED DIAZONIUM RING CLOSURE REACTIONS

### DeLos F. DeTar University of South Carolina

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### INTRODUCTION

In the middle eighteen nineties three groups of chemists independently discovered a new cyclization reaction of certain appropriately constituted diazonium salts. Fischer and Schmidt<sup>1</sup> reported that an aqueous

$$\begin{array}{c} CH_2 \\ CH_2 \\ CI^- \\ I \end{array}$$

solution of 2-benzylbenzenediazonium chloride (I) furnished fluore ne (II) on heating. Graebe and Ullmann² reported that 2-benzoylbe nzene-

<sup>&</sup>lt;sup>1</sup> Fischer and Schmidt, Ber., 27, 2786 (1894).

<sup>&</sup>lt;sup>2</sup> Graebe and Ullman, Ber., 27, 3483 (1894).

diazonium chloride (III) yielded fluorenone (IV), and Staedel<sup>3</sup> reported a somewhat similar result from the action of nitrous acid on 2,2'-diaminobenzophenone, a reaction that produced a little 1-hydroxyfluorenone. Two years later Robert Pschorr4 applied the ring closure reaction to the diazonium salt derived from trans-2-amino-α-phenylcinnamic acid (V) (aryl groups cis) to obtain phenanthrene-9-carboxylic acid (VI). The principal utility of these cyclization reactions has been the synthesis of substituted ring structures in which the positions of the substituents are In a series of papers Pschorr<sup>5-21</sup> reported the application of the reaction to the synthesis of a large number of phenanthrene derivatives with special emphasis on morphine degradation products. Although Pschorr was not the first to use the reaction, he was the first to exploit it extensively for the determination of structure. The phenanthrene synthesis, appropriately known as the Pschorr reaction, is still the best known of the various diazonium cyclization reactions. Various aspects of the cyclization reactions of diazonium salts have been reviewed previously.22-25

### MECHANISMS OF THE REACTIONS

### Comparison with the Gomberg-Bachmann Synthesis

Intermolecular analogs of the cyclization reactions have been recognized for many years. Pschorr4 pointed out their similarity to the biphenyl

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<sup>3</sup> Staedel, Ber., 27, 3362 (1894).
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<sup>&</sup>lt;sup>4</sup> Pschorr, Ber., 29, 496 (1896).

<sup>&</sup>lt;sup>5</sup> Pschorr, Wolfes, and Buckow, Ber., 33, 162 (1900).

<sup>6</sup> Pschorr, Ber., 33, 176 (1900). <sup>7</sup> Pschorr and Sumuleanu, Ber., 33, 1810 (1900).

<sup>&</sup>lt;sup>8</sup> Pschorr and Jaeckel, Ber., 33, 1826 (1900).

<sup>9</sup> Pschorr and Buckow, Ber., 33, 1829 (1900). 10 Pschorr, Seydel, and Klein, Ber., 34, 3998 (1901).

<sup>&</sup>lt;sup>11</sup> Pschorr and Schröter, Ber, 35, 2726 (1902).

<sup>12</sup> Pschorr, Seydel, and Stöhrer, Ber., 35, 4400 (1902).

<sup>13</sup> Pschorr and Vogtherr, Ber., 35, 4412 (1902). 14 Pschorr, Stählin, and Silberbach, Ber., 37, 1926 (1904).

<sup>&</sup>lt;sup>15</sup> Pschorr, Tappen, Hofmann, Quade, Schütz, and Popovici, Ber., 39, 3106 (1906).

<sup>16</sup> Pschorr and Busch, Ber., 40, 2001 (1907).

<sup>17</sup> Pschorr and Zeidler, Ann., 373, 75 (1910).

<sup>16</sup> Pschorr and Knöffler, Ann., 382, 50 (1911). 19 Pschorr, Selle, Koch, Stoof, and Treidel, Ann., 391, 23 (1912).

<sup>&</sup>lt;sup>20</sup> Pschorr, Zeidler, Dickhäuser, Treidel, and Koch, Ann., 391, 40 (1912).

<sup>&</sup>lt;sup>21</sup> Avenarius and Pschorr, Ber., 62, 321 (1929).

<sup>22</sup> Saunders, The Aromatic Diazo-compounds and Their Technical Applications, 2d ed.,

p. 254, Longmans, Green & Co., New York, 1949. 230 Holzach, Die Aromatischen Diazoverbindungen, p. 231, Ferdinand Enke, Stuttgart, 1947.

<sup>230</sup> Fieser and Fieser, Natural Products Related to Phenanthrene, 3rd ed., pp. 8, 29, Reinhold Publishing Co., New York, 1949.

<sup>24</sup> Leake, Chem. Revs., 56, 27 (1956).

<sup>25</sup> Hey and Osbond, J. Chem. Soc., 1949, 3164.

syntheses of Möhlau and Berger<sup>26</sup> which employed a diazonium salt, an aromatic solvent, and anhydrous aluminum chloride, and to those of

Kühling and of Bamberger<sup>27</sup> which were forerunners of the Gomberg-Bachmann reaction. More recently the analogy has generally been drawn with the Gomberg-Bachmann reaction itself<sup>28,29</sup> a typical example of which is the preparation of m-nitroblenzel by the reaction of m-nitrobenzel and alkali in a two-phase system.

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There are, however, a number of points of difference between the two-phase, alkaline, Gomberg-Baehmann reactions and the eyelization reactions. Many of the cyclization reactions, e.g. the fluorenone syntheses, are carried ont in acidic solutions. Such systems are initially single phase and only incidentally become multiphase owing to precipitation of reaction products. The Pschorr reaction is usually earried out in strongly acidic solution in the presence of copper powder. In a few cases it has been carried out in a homogeneous alkaline solution. Thus, in considering the mechanisms of the cyclization reactions, evidence concerning these intermolecular reactions is helpful but must be interpreted with due caution.

### Evidence for a Heterolytic Cyclization

Preliminary work on the mechanisms of the cyclization reactions<sup>30–31</sup> has shown that the fluorenone synthesis as usually carried out takes place by a heterolytic<sup>35</sup> (ionic) mechanism as shown in the equation. On the other hand, the copper-catalyzed Pschorr reactions may occur by a homolytic (free-radical) chain mechanism, though adequate evidence is

not yet available. The diazonium cyclization reactions therefore appear to belong to a lengthening list of reactions that occur by more than one mechanism

Evidence for a heterolytic fluorenone formation is derived from (1) general studies of the mechanisms of diazonium salt reactions and (2) specific studies of the fluorenone cyclization reaction.

There is good evidence based both on rate studies and on product studies with several diazonium salts that in water and in alcohols the thermal decomposition of the diazonium group is a heterolytic process under acidic conditions in the absence of light or of reducing agents, and that under alkaline conditions the decomposition takes place at least in part by homolytic processes.

The evidence for a heterolytic mechanism for the thermal decomposition of several diazonium salts in acidic aqueous solutions is based on the observation that the reaction is accurately first order over the full course  $(10-99\%)^{36-38}$  and is independent of the presence of or absence of a large variety of anions, or of acidity, over a considerable pH range. independence rules out various homolytic mechanisms involving hypothetical intermediate covalent diazo compounds such as the diazo chloride,  $C_6H_5N$ —NCl, or diazo hydroxide,  $C_6H_5N$ —NOH. The diazonium cation itself can give rise to radicals only by reactions yielding ionized nitrogen or water molecules and hence requiring prohibitively high energies. homolytic mechanisms are excluded by the kinetic evidence.

$$C_6H_5N_2^+ \to C_6H_5^{\cdot} + (\cdot N:::N:)^+$$
 $C_6H_5N_2^+ + H_2O \to C_6H_5^{\cdot} + (H:O:H)^+ + N_2$ 

Product studies show that benzenediazonium chloride reacts with methanol under acidic conditions to give high yields (90–95%) of anisole. $^{39}$ In the presence of sodium acetate the principal product is benzenc (85-90%), and the reaction is very sensitive to oxygen. Such results

<sup>&</sup>lt;sup>36</sup> DeTar and Ballentine, J. Am. Chem. Soc., 78, 3916 (1956).

<sup>&</sup>lt;sup>37</sup> DeTar and Kwong, J. Am. Chem. Soc., 78, 3921 (1956). 38 Moelwyn-Hughes and Johnson, Trons. Farodoy Soc., 36, 948 (1940).

<sup>39</sup> DeTar and Turetzky, J. Am. Chem. Soc., 77, 1745 (1955); 78, 3925, 3928 (1956).

require a homolytic mechanism in the presence of the acetate buffer and a heterolytic mechanism under acidic conditions.

In water the reaction of diazonium salts in the presence of alkali is highly complex, and the problem of unraveling mechanisms is difficult. However, the two-phase Gomberg-Bachmann reaction clearly requires some sort of homolytic mechanism as shown by the excellent orientation studies of Hey and his co-workers. The activating effect and the ortho-para directing effect of the nitro group of nitrobenzene afford perhaps the clearest single item of evidence in favor of a homolytic mechanism for the Gomberg-Bachmann reaction.

The fluorenone ring closure occurs readily under acidic conditions. Accordingly, a heterolytic mechanism seems most probable. This hypothesis is easily subject to further experimental investigation by use of appropriately substituted benzophenones in the ring closure reaction. The thermal decomposition of the diazonium salts derived from 2-aminobenzophenone in aqueous solution gave 65% of fluorenone and 35% of 2-hydroxybenzophenone, these two products together accounting quantitatively for the starting material. The product ratio and yield were insensitive to temperature in the range 25–75°. These products are ascribed to two competing heterolytic displacement reactions of the diazonium nitrogen; the one, intermolecular, involving a water molecule as the nucleophilic reagent and the other, intramolecular, involving an aryl group as the nucleophilic reagent.

Since a methyl group enhances and a nitro group diminishes the nucleophilic capabilities of the aryl ring, a methyl group should increase and a nitro group decrease the yield of fluorenone if the reaction is heterolytic. But, since the nitro group is an activating group for homolytic substitution reactions,<sup>40</sup> the ring closure should be more favored

$$\begin{array}{c} O \\ O \\ VIII \\ VIII \\ \end{array} \rightarrow \begin{array}{c} O \\ O \\ IX (61\%) \\ \end{array} \rightarrow \begin{array}{c} O \\ CH_3 \\ \end{array} + \begin{array}{c} O \\ OH \\ X (34\%) \\ \end{array} \rightarrow \begin{array}{c} O \\ CH_3 \\ \end{array} \rightarrow \begin{array}{c} O \\ IX (34\%) \\ \end{array}$$

<sup>40</sup> Augood, Cadogan, Hey and Williams, J. Chem. Soc., 1953, 3412, and earlier papers. See also DeTar and Scheifele, J. Am. Chem. Soc., 73, 1442 (1953); Dannley and Gippin, ibid., 74, 332 (1952); Rondestvedt and Blanchard, ibid., 77, 1769 (1955).

with the nitro derivative if the reaction is homolytic. The yields given in the equations show that the methyl group of VIII is without effect, though the nitro group of XI does diminish the fluorenone yield. The results are, therefore, in satisfactory agreement with predictions based on a heterolytic mechanism for the ring closure. The small effect of the substituents on the product ratio and yield, kinetic evidence, and certain other product evidence have been cited<sup>31</sup> as favoring an  $S_N$ 1 loss of nitrogen rather than an aromatic  $S_N$ 2 type of replacement.

### Products of the Homolytic Reaction

Under alkaline conditions the diazonium salts derived from 2-aninobenzophenone can be expected to react to some extent by a mechanism involving homolytic C—N bond cleavage. With alkali present (pH 12), only about 25% of fluorenone is produced. A similar reduction in yield under alkaline conditions has been observed for many of the diazonium cyclization reactions. In view of the demonstrated simultaneous occurrence of heterolytic and homolytic mechanisms, 39 it is not at all certain that even these low yields of fluorenone have resulted from free-radical intermediates.

The usual hypothesis about the mechanistic details of the homolytic Gomberg-Bachmann reaction is shown in the equation. The substituting radical is pictured as adding to the aromatic ring to give the new radical

XIV which loses a hydrogen atom to some other radical present in the solution. The intramolecular version of this step (XV  $\rightarrow$  XVI) might

be expected to occur even more readily by virtue of the proximity of the radical to the potential reaction site. Reactions in which there is closure of a five-membered ring usually occur much more readily than their intermolecular counterparts. For some unknown reason the o-benzoylphenyl radical (XV) does not undergo this cyclization reaction at all readily in comparison with competing reactions. Treatment of diazotized

2-amino-4'-methylbenzophenone (VIII) with alkali and with earbon tetrachloride leads to 3-methylfluorenone (IX), 2-chloro-4'-methylbenzophenone (XVII), and 2-chloro-4-methylbenzophenone (XVIII).<sup>33,34</sup> The 2-(4'-methylbenzoyl)phenyl radical (XIX) evidently reacts with earbon

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tetrachloride to abstract a chlorine atom to give 2-chloro-4'-methylbenzophenone (XVII) and with itself by an intramolecular chain transfer step to give the isomeric radical XX, which leads to 2-chloro-4-methylbenzophenone (XVIII). Even if all of the 3-methylfluorenone is ascribed to free-radical cyclization of XIX or XX, the free-radical cyclization is a relatively inefficient process. The ehlorobenzophenones XVII and XVIII are not expected from a carbonium ion intermediate. Although the general possibility of chlorine abstraction from carbon tetrachloride by a carbonium ion intermediate has perhaps not yet received a really rigorous investigation, the formation of the chlorobenzophenone XVIII from the earbonium ion VII is unlikely in view of the ease with which this ion cyclizes. Further evidence pointing to inefficiency of the free-radical cyclization step is the fact that the Gomberg-Bachmann reaction of diazotized 2-aminobenzophenone with benzene in the presence of alkali gives a 20% yield of 2-phenylbenzophenone (XXI) and little fluorenone. If these reactions are formulated as radical substitution processes, it is strange

$$\begin{array}{c|c}
O & O \\
C & & O \\
C_6H_6,NaOH
\end{array}$$

$$\begin{array}{c|c}
C_6H_5 & & \\
NNI & & \\
\end{array}$$

that an intermolecular reaction should take precedence over an intramolecular one, especially since the carbonyl group is expected to aid the cyclization process, for the carbonyl group is probably an activating group for free-radical substitution reactions. 40

Preliminary studies of the Pschorr reaction with the diazonium salt derived from cis-2-aminostilbene (XXII) have provided results quite different from the above.32 The thermal decomposition in aqueous solutions gives low yields of nitrogen and of phenanthrene (15-40%), the yields being higher at 100° than at 25°. A search was made for a nitrogen-containing by-product which was thought likely to be 3-phenylcinnoline. The product turned out to be indazole (XXIII). Several workers had previously reported benzaldehyde in reactions of this type, but no one had isolated the other cleavage fragment.41-43 These results then seem to typify the heterolytic process in the phenanthrene series.

If copper powder is present, the reaction is faster and the phenanthrene yield is higher (60-85%). It may be that the copper is promoting a homolytic reaction as has been suggested by Waters,28 or perhaps some quite different intermediate steps are involved. The assumption of a homolytic process finds some support in work on the mechanism of the reduction of diazonium salts with hypophosphorous acid, a free-radical chain reaction that is initiated by copper.44 Treatment of diazotized cis-2-aminostilbene with hypophosphorous acid leads to phenanthrenc, not to cis-stilbene. 42 Furthermore, sodium hypophosphite and copper powder have been used in a number of Pschorr reactions. Examples are to be found in Table I.

### SCOPE AND LIMITATIONS

### Examples of Different Types of Bridge

The diazonium cyclization reaction has been carried out with compounds having a number of different types of bridge. To the examples already mentioned (I, III, and V) may be added compounds XXIV-XXXIII.

<sup>&</sup>lt;sup>41</sup> Sachs and Hilpert, Ber., 39, 899 (1906); Ullmann and Gschwind, Ber., 41, 2291 (1908). 42 Ruggli and Staub, Helv. Chim. Acta, 19, 1288 (1936); 20, 37 (1937).

<sup>43</sup> Simpson, J. Chem. Soc., 1943, 447.

<sup>44</sup> Kornblum, Cooper, and Taylor, J. Am. Chem. Soc., 72, 3013 (1950).

(The percentages following the Roman numerals indicate the yield of normal Pschorr eyclization products.)

For the success of the cyclization reaction the carbon atoms that are to be linked together must be near each other. Perhaps the most favorable bridging group is the rigid ethylenic bridge of a cis-2-aminostilbene derivative (V and XXII). The corresponding trans ethylenic derivative undergoes other reactions typical of the diazonium group, 32, 42 but is quite

$$\stackrel{\text{Aq. II}_2\text{SO}_4}{\longrightarrow} + \stackrel{\text{CH}}{\longrightarrow} \text{NH}$$

- 45 Forrest and Tucker, J. Chem. Soc., 1948, 1137.
- 44 Cullinane, Rees, and Plummer, J. Chem. Soc., 1939, 151.
- 47 Hey and Mulley, J. Chem. Soc., 1952, 2276.
- 44 Heacock and Hey, J. Chem. Soc., 1952, 1508.
- 49 Schetty, Helv. Chim. Acta, 32, 24 (1949).
- 18 Barger and Weitnauer, Helv. Chim. Acta, 22, 1036 (1939).
- <sup>21</sup> Marion and Grassie, J. Am. Chem. Soc., 66, 1290 (1944).

incapable of giving phenanthrene. Hey and Mulley have calculated the distance of closest approach between the two relevant carbon atoms for several compounds (1.5 Å for V and XXII, 2.0 Å for XXIX, 2.2 Å for I. and 2.4 Å for III).47 The calculated values are rather sensitive to the angle of the C-X-C bond of the bridge; unfortunately this angle is not accurately known for most of the systems of interest, and hence present calculations cannot be expected to have quantitative significance. However, the estimates do clearly show that the stilbene derivatives have the most favorable spacing. There is a definite decline in yield of cyclic product with increasing bridge size as in the sulfide XXVII and the sulfone XXVIII, while the still larger selenide XXXIII gave only traces of cyclic product. Electrical factors seem to play a somewhat secondary role. The decrease in yield from 65% for fluorenone (IV) or for 3methylfluorenone (IX) to 35% for the nitrofluorenones (XII) $^{31}$  is important practically, but relatively small as such effects go. (Compare the factor of about a million in the difference in the rates of nitration of benzene and of nitrobenzene.) For the most part the data available are insufficient to permit an appraisal of the importance of the electrical effect of the groups present. Generally such effects may be neglected in planning a synthesis.

However, there is one electrical effect that seems to be of some importance. When a hydroxyl group is ortho to a diazonium group, a diazo oxide is formed (XXXIV). An ortho-quinoid structure is a possible resonance form even if the oxygen atom is part of an ether (XXXV). Similar structures are possible with ortho amino groups. Such structures may be responsible for resin-forming side reactions that often occur with compounds such as XXVI and XXXVI containing an oxygen atom or a nitrogen atom ortho to the diazonium function.<sup>52</sup>

### Side Reactions

Because the diazonium group is highly reactive, a number of reactions with external reagents can compete successfully at the expense of the cyclization. Examples of four such reactions follow.

<sup>52</sup> Ullmann and Gross, Ber., 43, 2694 (1910).

Replacement of the Diazonium Group by Hydroxyl. This reaction is always a potential competitor. Examples are the formation of 2-hydroxy-4'-methylbenzophenone (X) and 2-hydroxy-3'-nitrobenzophenone (XIII), both of which were mentioned earlier (p. 414).

Replacement of the Diazonium Group by Hydrogen. This occurs in the presence of reagents known to promote such a replacement. For example, sodium hypophosphite and copper convert diazotized cis-2-aminostilbene (XXII) into phenanthrene in an 80% yield. 42 However, this combination is of little use outside the phenanthrene series since diazonium salts less susceptible to ring closure give the normal replacement by hydrogen. 44 Diazotized sym-2-aminodiphenylethane (XXIV) is thus converted into sym-diphenylethane rather than into 9,10-dihydrophenanthrene. 42 The use of alcohols as solvents also can lead to reduction. 53 A copper suspension in aqueous or in organic media sometimes gives reduction products even though such obvious hydrogen sources as the alcohols are absent. 54,55

Replacement of the Diazonium Group by Halogen. The Gattermann reaction usually does not occur, but can compete if excess hydrochloric acid is present. A recently suggested procedure involving formation and decomposition of a triazene sometimes gives chlorine-containing by-products.<sup>25</sup>

Coupling of the Aryl Groups. The Vorländer-Meyer<sup>56</sup> coupling of diazonium salts leads either to biphenyl derivatives or to azobenzene derivatives. Ammoniacal cuprous hydroxide is one of the best reducing agents for the coupling reaction when this reaction is desired. The coupling side reaction has not usually been reported, but may well be the cause of some of the low yields obtained.

In addition to side reactions due to external agents, there are a number of side reactions that can occur intramolecularly.

Formation of Xanthones. An alkoxyl group in the 2'-position interferes with many of the cyclization reactions. In the fluorenone series the product is a xanthone derivative, e.g. XXXVII, 57-59 rather

than a fluorenone derivative. The failure of diazotized trans-2-amino- $\alpha$ -(2'-furyl)cinnamic acid (XXXVIII) to give identifiable products may have

been a result of the occurrence of reaction at the oxygen atom rather than at the 3-position of the furan ring.<sup>60</sup>

Elimination of Carboxyl and Nitro Groups. Examples of the elimination of 2'-nitro groups and of 2'-earboxyl groups have been reported. The 2'-nitro group of diazotized 2-amino-2'-nitrobenzophenone (XXXIX) is eliminated to an appreciable extent.<sup>47</sup> The 2'-nitro group of 2-amino-2'-nitro-N-methyldiphenylamine (XL) is largely eliminated if copper

powder is used in the decomposition of the diazonium salt, and largely retained if the copper is omitted.<sup>47</sup> Thermal decomposition in aqueous sulfuric acid solution of the diazonium salt derived from 2-amino-2'earboxybenzophenone (XLI) in the absence of eopper led to approximately 10% yields each of fluorenone and of fluorenone-1-earboxylie acid (XLII).61 Side reactions of these types seem to be less important in the phenanthrene series, though detailed product studies have yet to be made. Thus several 1-methoxy- and 1-earboxy-phenanthrene derivatives (XLIII-XLV) have been prepared by the Psehorr reaction. 5,15,62

Deamination in Phenanthridone Syntheses. An intramolecular hydrogen abstraction and resultant demethylation reaction has been reported 63,64 in an attempted preparation of 4-substituted phenanthridones from 2-substituted N-(2'-aminobenzoyl)-N-methylanilines. 65 Incidentally the phenanthridone ring closure has usually been unsuccessful if

$$\begin{array}{c} \text{CO-NCH}_3 & \longrightarrow \text{ArN}_2\text{+HSO}_4\text{-} \xrightarrow{\text{Warm}} & \text{CO-NH} \\ \hline \text{NH}_2 & & & \text{NO}_2 \\ \hline \end{array}$$

$$\longrightarrow \text{ArN}_2\text{+BF}_4\text{-} \xrightarrow{\text{Gu powder}} & & \text{25\%} \\ \hline \end{array}$$

$$[63, 65]$$

the amino group is not in the benzoyl ring; the amide XLVI gave no phenanthridone. 66

<sup>61</sup> Sieglitz, Ber., 57, 316 (1924).

<sup>62</sup> Hill and Short, J. Chem. Soc., 1937, 260.

<sup>63</sup> Hey and Turpin, Chemistry & Industry, 216, 216, 221 (1954). 64 Forrest, Haworth, Pinder, and Stevens, J. Chem. Soc., 1949, 1311.

<sup>65</sup> Heaeoek and Hey, J. Chem. Soc., 1953, 3.

<sup>66</sup> Chardonnens and Würmli, Helv. Chim. Acta, 33, 1338 (1950).

	,

Simpson<sup>43</sup> has discussed in admirable fashion the factors that lead to cinnoline formation rather than to carbon cyclization. The diazonium salt derived from cis-2-(1'-naphthyl)-1-(2"-aminophenyl)-1-phenylethene

$$H_{2}N$$

$$\xrightarrow{Aq. CH_{3}CO_{2}H}$$

$$H_{2}SO_{4}-NaNO_{2}$$

$$Room$$

$$temp.$$

$$LIII$$

$$LIV$$

(LI) reacted on warming to give 2-phenylehrysene (LII). The presence or absence of 9-(1'-naphthylmethylene)fluorene (LIII) was not ascertained. At room temperature 3-(1'-naphthyl)-4-phenyleinnoline (LIV) was the major product. Cinnoline formation, like the indazole (XXIII) production observed with diazotized cis-2-aminostilbene (XXII), evidently has a lower activation energy than does loss of nitrogen, for nitrogen elimination is favored by high reaction temperatures. In general, the presence on the ethylenie bridge of electron-releasing groups aids and the presence of electron-attracting groups hinders einnoline formation. With a carboxyl group present on the bridge, einnoline formation does not occur.

Cinnoline ring closure occurs if an active methylenic bridge is present; the ketone LV gives the cinnoline LVI rather than the phenanthrol LVII.

If a secondary amino group is in a position to form a five- or sixmembered ring by coupling with the diazonium group, the coupling will usually take place in preference to loss of nitrogen. Examples are the formation of the triazine derivative LVIII from diazotized 2-amino-

benzanilide, <sup>68</sup> the formation of the thiatriazine derivative LIX from diazotized 2-aminobenzenesulfonanilide, <sup>52</sup> and the formation of 1-phenylbenzotriazole (LXI) from diazotized 2-aminodiphenylamine. <sup>69</sup> Carbon cyclization has been achieved in two of the examples. If the diazotized 2-aminobenzenesulfonanilide is heated, the sultam (LX) of 2'-aminobiphenyl-2-sulfonic acid is obtained. Furthermore, many 1-arylbenzotriazoles such as LXI are converted to carbazole derivatives with loss of nitrogen when they are heated to 250–400°.

### Factors Affecting the Direction of Ring Closure

In the cyclization reaction there are sometimes two or more possible products of the ring closure. Such possibilities always arise when substituents in the 3'- and 5'-positions of the aryl ring to which closure is made are not identical, providing that both the 2'- and the 6'-positions are free. Examples are given in the equations. Such reactions are usually to be avoided.

<sup>&</sup>lt;sup>68</sup> König and Reissert, Ber., 32, 782 (1899). See, also, Pictet and Gonset, Arch. sci. phys. nat. Genève. [4] 3, 37 (1897) (Chem. Zentr., 1897, I, 413).

<sup>69</sup> Graebe and Ullmann, Ann., 291, 16 (1896).

TSCHORK STRINESIS AND Glosses.

$$CO_{2}H$$

$$CH_{3}$$

$$CH_{3}O$$

$$CH_{3}O$$

$$CH_{3}O$$

$$CH_{3}O$$

$$CH_{3}O$$

$$CH_{3}O$$

$$CH_{3}O$$

$$CH_{4}O$$

$$CH_{3}O$$

$$CH_{5}O$$

$$CH_{3}O$$

$$CH_{5}O$$

$$CH_{5}O$$

$$CH_{5}O$$

$$CH_{5}O$$

$$CH_{5}O$$

$$CH_{5}O$$

$$CH_{5}O$$

$$CH_{5}O$$

$$CH_{5}O$$

$$CO_{2}H$$

$$CH_{2}O$$

$$CH_{3}O$$

$$CO_{2}H$$

$$CH_{3}O$$

$$CH_{3}O$$

$$CO_{2}H$$

$$CO_$$

In the phenanthrene series considerable use has been made of bromine 72,73 in the 6'-position as a blocking group, the bromine being removed eventu-Although the phenanthrene ring can be formed with ally by reduction.

<sup>70</sup> Mayer and Balle, Ann., 403, 167 (1914).

<sup>&</sup>lt;sup>71</sup> Späth and Tharrer, Ber., 66, 904 (1933).

<sup>72</sup> Girardet, Helv. Chim. Acta, 14, 513 (1931).

<sup>73</sup> Lewis and Elderfield, J. Org. Chem., 5, 290 (1940).

two alkoxyl groups in the 4- and 5-positions as shown by LXII and LXIII, two alkyl groups in the 4- and 5-positions are too bulky to permit closurc. No identifiable product was obtained from the reaction of diazotized

trans-2-amino-3-methyl- $\alpha$ -(2'-bromo-5'-methylphenyl)cinnamic acid (LXIV). (The acid LXV was not formed.) It is possible to use this effect to advantage in preparing dialkylphenanthrene derivatives. Diazotized trans-2-amino-3-methyl- $\alpha$ -(3'-ethylphenyl)cinnamic acid (LXVI) gave a good yield of 7-ethyl-4-methylphenanthrene-9-carboxylic acid (LXVII), uncontaminated with the 4,5-isomer.

With a 1-naphthyl group in the  $\alpha$ -position of the cinnamic acid, closure takes place in the 2-position rather than in the 8-position. trans-2-Amino- $\alpha$ -(1'-naphthyl)cinnamic acid (LXVIII) when diazotized and treated with copper powder and sodium hypophosphite gave chrysene-5-carboxylic

<sup>74</sup> Fieser and Joshel, J. Am. Chem. Soc., 62, 1211 (1940).

<sup>75</sup> Lothrop and Goodwin, J. Am. Chem. Soc., 65, 363 (1943).

acid (LX1X). The 1-naphthyl ketone LXX in which the 2-position is blocked does, however, give a small yield of the 1,8-cyclization product LXX1.

With a 2-maphthyl group, closure takes place to the I-position in preference to the 3-position. This is illustrated by the reaction of diazotized trans-2-amino-x-(2'-maphthyl)cinnamic acid (LXXII) to give primarily benzo[e]phenauthrene-6-carboxylic acid (LXXIII).<sup>76</sup>

### Simultaneous Closure of Two Rings

A few examples of the simultaneous closure of two rings have been reported. The m-phenylenediacetic acid derivative LXXV gave dibenz-[aj]anthracene-6,8-dicarboxylic acid (LXXVI) and 2,2'-diamino-6,6'-diphenylbiphenyl (LXXVII) gave dibenzo[el]pyrene (LXXVIII).

$$\begin{array}{c|c}
CO_2H & CO_2H \\
NH_2 & CO_2H \\
NH_2 & LXXVI \\
NH_2 & LXXVII
\end{array}$$

$$[78]$$

<sup>76</sup> Cook, J. Chem. Soc., 1931, 2524.

 <sup>&</sup>lt;sup>77</sup> Cook, J. Chem. Soc., 1932, 1472.
 <sup>78</sup> Sako, Bull. Chem. Soc. Japan, 9, 55 (1934) [C. A., 28, 3730 (1934)].

### Aliphatic Analogs

Simple aliphatic amines appear not to undergo ring closure. Geissman and Tess<sup>79</sup> report that the treatment of 2-aminomethylbiphenyl (LXXIX) with sodium nitrite in aqueous acctic acid yields 2-biphenylmethanol. The details reported do not seem to exclude entirely the possibility of some fluorene production. The action of nitrous acid on 3-phenylpropylamine

(LXXX) does not seem to give any indane. BO However, a very interesting ring elosure involving 2-(2'-naphthyl)diazoaeetophenone (LXXXI) to give 6-ehrysenol (LXXXII) has been reported by Cook and Schoental. BI

$$\begin{array}{c|c} O \\ N_2CH \\ \hline \\ N_2CH \\ \hline \\ In CH_2CO_2H \\ \hline \\ LXXXII \\ \end{array}$$

This reaction almost surely involves an intermediate aliphatic diazonium salt.

### EXPERIMENTAL CONDITIONS

### Preparation of the Amines

The most troublesome aspect of most of the diazonium cyclization reactions is the preparation of the amine having the desired structure. Each of the different types of bridge systems requires a separate approach.

Pschorr Reaction Intermediates. The cinnamie acids required for the Pschorr reaction are generally obtained by a Perkin condensation

<sup>79</sup> Geissman and Tess, J. Am. Chem. Soc., 62, 514 (1940).

<sup>80</sup> Fort and Roberts, J. Am. Chem. Soc., 78, 584 (1956).

<sup>81</sup> Cook and Schoental, J. Chem. Soc., 1945, 288.

using o-nitrobenzaldehyde or a substituted o-nitrobenzaldehyde. The reaction is illustrated by the preparation of trans-2-nitro-α-phenyleinnamic acid (LXXXIII).32,82

Psehorr originally specified the use of fused zine chloride in this reaction, but its presence appears to be detrimental<sup>83</sup> although many succeeding workers have followed the original procedure. For the condensation of o-nitrobenzaldchyde with phenylacetic acid, potassium carbonate proved a more convenient catalyst than potassium phenylacetate, and it gave the same yield. Small amounts of acctic acid or moisture had no effect on the yield.

Fortunately, the presence of the carboxyl group leads to the formation of more of the trans-cinnamic acid with the aryl groups in the proper cis relationship than of its undesired stereoisomer. A discussion of the preparation of the o-nitrobenzaldehydes and of the phenylacetic acid derivatives is beyond the scope of this chapter. Examples of such preparations are available in many of the references cited in Table I.

A few nitrocinnamic acids such as LXXXIV have been prepared from

o-nitrophenylacetic acid, 70 which is readily available from o-nitrotoluene. Condensation of o-nitrotolucne with diethyl oxalate in the presence of sodium methoxide followed by hydrolysis gives o-nitrophenylpyruvio acid, which is readily oxidized to o-nitrophenylacetic acid with hydrogen peroxide.84

The most satisfactory reducing agent for the nitro group is an ammoniacal suspension of ferrous hydroxide. The hydrated iron oxides are readily removed. Catalytic hydrogenation is difficult to control and often leads to partial reduction of the ethylenic bond.

Some of the amino acids exhibit an interesting polymorphism, 4,84a Crystallization of trans-2-amino-α-phenyleinnamic acid from othyl acotato leads to a bright yellow modification, m. p. 186–187°, whereas crystallization from ethanol gives colorless prisms sintering at 170° to give the yellow form which then melts at 185-187°.

Several cis-stilbene derivatives have been obtained by decarboxylating the cinnamic acid derivatives using the copper chromite hydrogenation

<sup>82</sup> DeTar, Org. Syntheses, 35, 89 (1955). 83 Bogert and Stamatoff, Rec. trav. chim., 52, 584 (1933).

<sup>84</sup> May and Mossetig, J. Org. Chem., 11, 435 (1946).

<sup>84</sup>a Gulland and Virden, J. Chem. Soc., 1928, 1478.

catalyst in refluxing quinoline.32,42,85 Rearrangement to the trans isomer occurs to only a relatively minor extent during the decarboxylation.

Intermediates for Dihydrophenanthrenes. Catalytic reduction of the 2-nitro-α-phenylcinnamic acids leads to the formation of sym-2aminodiphenylethane derivatives. Another method utilizes the condensation of p-methoxybenzaldchyde with oxindole, followed by eatalytic

reduction to give 3-(4'-methoxybenzyl)oxindole (LXXXV). The oxindole LXXXV can be hydrolyzed by aqueous barium hydroxide at 170-180°, to give α-(2-aminophenyl)-β-(4'-methoxyphenyl)propionic acid.86 A third synthesis utilizes the condensation of a benzyl chloride with a phenylacetonitrile as in the preparation of LXXXVI.87 The nitro

$$\begin{array}{c} \text{CH}_3\text{O} \\ \text{CH}_3\text{O} \\ \text{CH}_3\text{O} \\ \text{CH}_3\text{O} \end{array} + \begin{array}{c} \text{CH}_2\text{CN} \\ \text{OCH}_3 \end{array} \xrightarrow{\begin{array}{c} \text{C}_2\text{H}_5\text{ON}_2 \\ \text{C}_2\text{H}_5\text{OH} \end{array}} \xrightarrow{\begin{array}{c} \text{CH}_3\text{O} \\ \text{CH}_3\text{O} \\ \text{CH}_3\text{O} \\ \end{array}} \xrightarrow{\begin{array}{c} \text{CH}_3\text{O} \\ \text{CH}_3\text{O} \\ \end{array}} \begin{array}{c} \text{CN} \\ \text{CH}_3\text{O} \\ \end{array}$$

compound was reduced catalytically with 2% palladium on strontium earbonate in dioxane solution.

Intermediates for Fluoranthenes. The required 1-(2'-nitrophenyl)naphthalene is usually obtained by a mixed Ullmann biaryl synthesis, as

85 DeTar and Carpino, J. Am. Chem. Soc., 78, 475 (1956).

87 Cook, Dickson, Ellis and Loudon, J. Chem. Soc., 1949, 1074.

<sup>86</sup> Windaus and Eickel, Ber., 57, 1871 (1924). Compare, Kirchnor, Nachr. Akad. Wiss. Göttingen, 1921, 154 (Chem. Zentr., 1923, I, 944).

illustrated for the preparation of 1-(2'-nitro-4'-methylphenyl)naphthalene (LXXXVII); this product was isolated by a combination of distillation and chromatography and was hydrogenated catalytically using Raney nickel.88

Intermediates for the Preparation of N-Substituted Carbazoles and Dibenzofurans. The required 2-aminodiphenylamine or 2-aminodiphenyl ether is obtained by either catalytic or chemical reduction of the corresponding nitro compound,30,89 the latter being obtained from an appropriate o-chloro- or o-bromo-nitrobenzene by reaction with an

aniline derivative 47 or with a phenolate salt. 90 The purpose of the copper new 1 is less that of a copper powder in the 2-nitrodiphenyl ether preparation is less that of a catalyst than a catalyst than of an inhibitor. In the absence of the copper, an exothermic reaction to a continuous state of the copper to exidation of reaction to the copper to exidation of reaction to the copper to exidation of reaction to the copper to exidation of the copper to exide the copp reaction takes place leading to a black resin, due perhaps to oxidation of the phenolar residence of the copper. the phenol by the nitro compound.

Intermediates for Fluorenones. The preparation of 2-aminobenzophenones has been reviewed. One useful method starts with anthropity anthranilic acid. 92 The amino group is protected with a p-toluenesulfonyl group and 11 group, and then a Friedel-Crafts synthesis is carried out on the carboxyl function as " function as illustrated in the preparation of LXXXVIII. p-toluenesulfonyl group is removed by acid hydrolysis. By this procedure

7-toluenesulfonyl group is removed by the Pols, 
$$Co_2H$$
 
$$CO_2H$$
 
$$NHSO_2C_6H_4CH_3$$
 
$$O$$
 
$$NH$$
 
$$CH_3$$
 
$$SO_2C_6H_4CH_3$$
 
$$LXXXVIII$$

<sup>88</sup> Tucker and Whalley, J. Chem. Soc., 1949, 3213.

<sup>\*\*</sup> Gilman and Broadbent, J. Am. Chem. Soc., 69, 2053 (1947).

\*\*\* Gilman and Broadbent, J. Am. Chem. Soc., 69, 2053 (1947).

\*\*\* Gilman and Broadbent, J. Am. Chem. Soc., 69, 2053 (1947).

ouman and Broadbent, J. Am. Chem. Soc., 69, 2003 (1943).

Browster and Groening, Ory. Syntheses Coll. Vol. 2, P. 445 (1943).

Simport Advisor And Groening, Ory. Syntheses Coll. Vol. 2, P. 445 (1943). <sup>91</sup> Simpson, Atkinson, Schofield, and Stephenson, J. Chem. Soc., 1945, 646.

<sup>&</sup>lt;sup>92</sup> Ullmann and Bleier, Ber., 35, 4273 (1902).

2-aminobenzophenone and 2-amino-4'-methylbenzophenone are obtained in a 50% over-all yield from anthranilic acid.93

Unfortunately o-nitrobenzoyl chloride gives very poor yields in Friedel-Crafts reactions.<sup>54</sup> o-Chlorobenzoyl ehloride reacts normally, but ammonolysis of the halogen is difficult.94 On the other hand the o-earboxyl group of o-benzoylbenzoic acids can usually be converted to an amino group via the Hofmann or the Curtius reaction. 95,96

An interesting oxidation of indole derivatives obtained from phenyl-

hydrazones by the Fischer indole synthesis makes available a number of hitherto inaccessible 2-aminobenzophenones.94

### The Cyclization Reaction

The amine is usually diazotized in aqueous sulfuric acid. Insoluble or unreactive amines have been diazotized in acctic acid, methanol, or ethanol with butyl nitrite and sulfuric acid or hydrochloric acid. Amino acids are often dissolved in alkaline solutions along with sodium nitrite, the mixture being run into sulfuric acid.

The numerous methods for bringing about cyclization by decomposition of the diazonium salt fall into a relatively few classes. Although some comparative quantitative data are available on the efficiency of these cyclization procedures, it is necessary in most cases to rely on the evaluation of semiquantitative preparative runs.

Method 1. The diazonium salt solution is merely heated. This procedure nearly always gives some of the cyclization product if cyclization

<sup>93</sup> DeTar and Scheifele, Org. Syntheses, 32, 8 (1952).

<sup>94</sup> Schofield and Theobald, J. Chem. Soc., 1950, 1505.

<sup>95</sup> Graebe and Ullmann, Ann., 291, 8 (1896).

<sup>96</sup> Wallis and Lane, in Adams, Organic Reactions, Vol. III, 267, John Wiley & Sons, New York, 1946; Smith, ibid., 337.

is structurally possible. In the fluorenone series the use of 50% sulfuric acid gives somewhat better yields of the fluorenone and less of the hydroxy-benzophenone than does 1 N sulfuric acid. To Concentrations of sulfuric acid greater than 75% tend to give lower yields of 3-methylfluorenone, probably because of sulfonation (however, cf. the preparation of 2-nitrofluorenone below, p. 438). For the production of phenanthrene this method is definitely inferior to Method 2 using copper powder. 22

Method 2. The diazonium salt solution is heated in the presence of copper powder. Gattermann copper<sup>98</sup> prepared by reducing cupric sulfate with zinc dust has been used frequently, though other types of copper may be as good or better. The use of copper powder in the presence of alcoholic solvents is inadvisable except for the phenanthrene cyclization. In other systems the procedure leads to extensive replacement of the diazonium group by hydrogen.

For 2-(4'-methylbenzoyl)benzenediazonium salts, thermal decomposition in 1 N sulfuric acid gave 65% of 3-methylfluorenone, while copper powder in 1 N sulfuric acid gave a 50% yield and led to the formation of some 4-methylbenzophenone. In 50% sulfuric acid an 80% yield of cyclic product was produced whether or not copper or solid cuprous chloride was present. On the other hand 2-(3'-nitrobenzoyl)benzenediazonium salts gave a 35% yield of cyclic product in 1 N sulfuric acid and a 55% yield in 50% sulfuric acid, but with copper powder present a 95% yield of cyclic product was formed in 1 N sulfuric acid and an 85% yield in 50% sulfuric acid. From 2 to 5% of 3-nitrobenzophenone was also produced when copper powder was present. The above results were obtained with crystalline diazonium salts and are based on quantitative chromatographic isolation of the fluorenone-benzophenone mixtures, these being analyzed by their infrared absorption spectra. 97

Method 3. The diazonium salt solution is made alkaline and heated. In most cases this method gives poor results. It has been used successfully with some Pschorr cyclizations and may have particular merit if there is a hydroxyl group ortho to the diazonium group (resulting in the formation of a relatively stable diazo oxide rather than a diazonium salt).

Method 4. The diazonium salt solution is treated with sodium hypophosphite and copper. This procedure is usable only with the Pschorr cyclization. In all other cases it leads to replacement of the diazonium group by hydrogen. This procedure was first described by Ruggli and Staub<sup>42</sup> and appears to have become fashionable, although there does not appear to be any information about its merit in comparison with Method 2.

<sup>&</sup>lt;sup>97</sup> DeTar and Whiteley, J. Am. Chem. Soc., 79, in press (1957).

<sup>98</sup> Gattermann, Ber., 23, 1219 (1890).

Other Methods. In a few examples the erystalline fluoborate has been suspended in acetone and stirred with copper powder.25 The method may prove to be of advantage in some eases, but the reported high yields are mostly based on the fluoborate. Yields calculated on the basis of the amine are less attractive.

Another method eonsists of reaction of the diazonium salt with dimethylamine to give a triazine. The triazine is suspended in an organic solvent and treated with hydrogen ehloride. The reported examples seem to give relatively poor yields.25

The N-nitrosoamide decomposes on heating to give some eyelization product.25,982 This method also seems to be of no particular preparative use.

### EXPERIMENTAL PROCEDURES

- 1-Bromo-3,4-dimethoxyphenanthrene-9-carboxylic Acid. (Psehorr synthesis using Gattermann copper paste<sup>98</sup> in an aqueous acidie medium.)99
- (a) Preparation of the amine, trans-2-amino-6-bromo-3,4-dimethoxy-aphenylcinnamic acid. A mixture of 15 g. of 6-bromo-3,4-dimethoxy-2-nitrobenzaldehyde (6-bromo-2-nitroveratraldehyde), 8.3 g. of dry sodium phenylacetate, and 90 ml. of acetic anhydride is heated at 100° for thirty hours. Water (750 ml.) is added and, after hydrolysis of the excess anhydride, an excess of ammonia is added and the mixture extracted with two 400-ml. portions of ether. Acidification of the aqueous layer gives 13 g. of the crude nitrocinnamic acid which gives 10.7 g. of material, m. p. 193-200° after one crystallization from methanol. Recrystallization of the combined products of several runs gives the pure nitroeinnamic acid, m. p. 206-208° (30% yield). Reduction with ammoniacal ferrous sulfate gives the aminocinnamic acid in 98% yield.
  - (b) Cyclization. To a mixture of 2 g. of trans-2-amino-6-bromo-3,4-dimethoxy-α-phenylcinnamic acid, 20 ml. of ethanol, and 5.2 ml. of 3 N hydrochloric acid is added at  $0^{\circ}$  a 50% solution of butyl nitrite in ethanol. After one-half hour, the orange solution is diluted with 200 ml. of water, and copper paste is added in small portions with mechanical stirring.\* The mixture consisting of light green solution, copper powder, and a white solid, is extracted with ether. Sodium carbonate extraction of the ether followed by acidification of the extract gives 1.57 g. of 1-bromo-3,4-dimethoxyphenanthrene-9-carboxylic acid. The yield of partly purified product from several runs was 72-82%. After washing

<sup>98</sup>a DeTar and Savat, J. Am. Chem. Soc., 75, 7117 (1953).

<sup>99</sup> Small and Turnbull, J. Am. Chem. Soc., 59, 1541 (1937).

<sup>\*</sup> The quantity of copper paste is not specified in the original article, but the writer has found that quantities of the order of one gram are satisfactory.

with acetone followed by several recrystallizations from ethanol and from acetic acid, the product melts at 260-270° (evac. tube).

- 4,6-Dimethylphenanthrene-9-carboxyllc Acid. (Psehorr synthesis using 75% ethanol as the solvent with copper and sodium hypophosphite as promoters.)73
- (a) Preparation of the amine, trans-2-amino-3-methyl-α-(4'-methylphenyl) cinnamic acid. A mixture of 37.6 g. (0.2 mole) of potassium p-methylphenylacetate, 33 g. (0.2 mole) of 2-nitro-3-methylbenzaldehyde, and 204 g. (2 moles) of acetic anhydride is heated with stirring for eight hours at 105-110°. The anhydride is decomposed at 100° by eareful addition of water, and the reaction mixture is poured into 11. of cold 5% hydrochloric acid. The solid is recrystallized from acetic acid and then from ethanol to give 38 g. (65%) of the nitrocinnamic acid, m. p. 250.5-251.5°. A suspension of 36 g. of the nitro acid in 500 ml. of warm dilute aqueous ammonia is stirred into a boiling mixture of 240 g. of hydrated ferrous sulfate, 500 ml. of water, and 500 ml. of 12 M aqueous ammonia. Boiling is continued for an hour, and the mixture is allowed to stand overnight. The filtrate from the hydrated iron oxides is acidified to congo Red with hydrochloric acid. The resulting crude amino acid is recrystallized from 70% methanol to give 27.2 g. (84%) of product, m. p. 176.5-177.5°
- m. p. 176.5–177.5°.

  (b) Cyclization. A suspension of 15 g. of trans-2-amino-3-methyl-α-(4'-methylphenyl)cinnamic acid in 150 ml. of 15% ethanolic hydrogen (4'-methylphenyl)cinnamic acid in 150 ml. of freshly distilled amyl chloride is stirred for an hour at 0°, then 20 ml. of freshly distilled amyl chloride is stirred for an hour at 0°, then 20 ml. of freshly distilled amyl intrite is added and stirring continued for another hour. The solution is nitrite is added to a suspension of 1 g. of copper powder in a solution of 50 g. then added to a suspension of 1 g. of copper powder in a solution of sodium hypophosphite in 50 ml. of water containing 2 drops of concording the solution acid. A violent evolution of nitrogen occurs, and the centrated sulfuric acid. A violent evolution of nitrogen occurs, and the phenanthroic acid separates. After stirring for thirty minutes with phenanthroic acid separates. After stirring for thirty minutes with gentle heating, the solution is cooled and the acid collected and dissolved in sodium hydroxide solution. The filtered alkaline solution is acidified in sodium hydroxide solution. The filtered alkaline solution is acidified in sodium hydroxide solution. The filtered alkaline solution is acidified and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recrystallized from 80% and the 4,6-dimethyl-9-phenanthroic acid is recr
- colorless needles, m. p. 216–217°.

  3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 3-Chlorophenanthrene-9-carboxylic Acid. (Pschorr reaction via 4-Chlorophenanthrene-9-carboxylic Acid.)
- (a) Preparation of the amine, trans-4-chloro-α-(2'-aminophenyl)cinnamic acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g. of sodium o-nitrophenylacetate, 19 g. of p-chloro-acid. A mixture of 28 g

recrystallized from acctic acid to give the nitrocinnamic acid; 14.9 g., m. p. 196-199°. For reduction, 5.1 g. of the nitroeumamic acid is dissolved in 50 ml. of 4 M aqueous ammonia and added to a hot (80-90°) slurry prepared by addition of \$5 ml. of 12 M aqueous ammonia to a solution of 34 g. of ferrous sulfate in 102 ml. of water. After ten minutes the mixture is filtered through diatomaceous silien (Filter-Cel). Acidification gives 3.4 g. of the aminocinnamic acid. Attempted erystallization from ethanol gives the lactam, 4-chlorobenzaloxindole.

(b) Cyclization. To 80 ml. of 5 N sulfurie acid cooled to -3 to  $+2^{\circ}$ is added during twenty minutes a suspension of 5 g. of trans-4-chloro- $\alpha$ -(2'-aminophenyl)einnamic acid, 3 g. of sodium nitrite, 75 ml. of water, and 2 ml. of M aqueous ammonia. After an additional hour of stirring at 0 to 5°, 20-30 ml. of ethanol and 5 g. of copper-bronze are added, and the mixture is heated to 70-80° for one-half hour. The precipitate is collected on a filter and the alkali-soluble material leached from the copper with hot dilute sodium hydroxide. The alkaline filtrate on acidification gives crude 3-chlorophenanthrene-9-carboxylic acid, which on recrystallization from glacial acetic acid has a m. p. of 249-251°; vield 1.4 g.

2-Nitrofluorenone. (Fluorenone eyelization in concentrated sulfurie acid.)100 To a solution of 3 g. of 2-amino-5-nitrobenzophenone in 30 ml. of concentrated sulfuric acid, 1 g. of powdered sodium nitrite is added over a period of fifteen minutes at -5 to 0°. The solution is heated at 95° for two hours, then diluted with 60 ml. of water. The product on recrystallization from ethanol gives 1.7 g. (60%) of 2-nitrofluorenone, m. p. 220-221°, and 0.4 g. (13%) of 2-hydroxy-5-nitrobenzophenone, m. p. 119-121°.

With 85% sulfuric acid the yields are 56 and 16%, respectively; with 50% sulfuric acid and copper powder the yields are 15 and 6%.

11-Chrysofluorenone (LXXXIX). (Fluorenone synthesis, use of copper powder; diazotization with isoamyl nitrite.)101

LXXXIX

<sup>100</sup> Nunn, Schofield, and Theobald, J. Chem. Soc., 1952, 2797.

<sup>101</sup> Orchin and Reggel, J. Am. Chem. Soc., 73, 436 (1951). The authors give extensive details.

- (a) Preparation of the amine, 1-benzoyl-2-aminonaphthalene. 1-Benzoyl-2-benzoylaminonaphthalene is prepared from 99 g. of 2-benzoylaminonaphthalene and 160 ml. of benzoyl chloride at a temperature of 100-110°, adding 234 g. of stannic chloride as condensing agent during thirty minutes. The total reaction time is forty-five minutes. After hydrolysis, the product is isolated by crystallization from ethanol. A total of 104 g. (74%) of tan material, m. p. 155-157°, is obtained. 1-Benzoyl-2-aminonaphthalene is obtained in 93% yield by hydrolysis with potassium hydroxide in refluxing 80% ethanol for twelve to sixteen hours.
- (b) Cyclization. To a stirred solution of 50 g. of 1-benzoyl-2-aminonaphthalene in 1.5 l. of acetic acid containing 21 ml. of sulfuric acid is added in two minutes a solution of 53 ml. of isoamyl nitrite in 250 ml. of acetic acid. After thirty minutes, the solution is cooled in an ice bath and 25.5 g. of copper powder is added; reaction proceeds at ice temperature for thirty minutes, at room temperature for two and one-half hours, and at steam-bath temperature for three hours. The mixture is then allowed to stand overnight. Part of the acetic acid (1.21.) is removed by distillation, and the remaining solution is filtered and diluted with water. the tarry residue, by extraction, distillation, and crystallization, there is obtained 15 g. (33%) of 11-chrysofluorenone, m. p. 133.2-134.8°. No alkali-soluble product is found.

The above procedure has been carried out a number of times with consistent results. Variations in the procedure gave the following results: (a) on addition of copper at room temperature the mixture became hot and the yield dropped to 11%; (b) use of ethanol gave a very low yield; (c) addition of sodium hypophosphite with ethanol or acetic acid as solvent gave very low yields; and (d) use of half as much acetic acid gave a 26% yield.

2-Bromo-4-methyldibenzofuran. (Cyclization by heating acidic solution of diazonium salt.)102 (a) Preparation of the amine, 2-amino-4-bromo-6-methyldiphenyl ether. A mixture of 14.2 g. (0.048 mole) of 2,5-dibromo-3-nitrotoluene and 6.86 g. (0.052 mole) of potassium phenoxide is heated at 170° for three hours. The cooled mixture is treated with water, and the product is extracted with ether and recrystallized from petroleum ether (b. p. 60-68°) to give 12 g. (81%) of phenyl 2-nitro-4-bromo-6-methylphenyl ether, m. p. 92-94°. The nitro group is reduced by dissolving 12 g. (0.039 mole) of the nitro compound in 150 ml. of dry ether to which 20.85 g. (0.093 mole) of stannous chloride has been added, and then saturating the resulting solution with hydrogen chloride at 0°. The hydrochloride separates as a light brown solid (10.9 g.) which is diazotized without further purification.

<sup>&</sup>lt;sup>102</sup> Gilman, Van Ess, and Hayes, J. Am. Chem. Soc., 61, 643 (1939).

- (b) Cyclization. The diazonium solution is added slowly to 150 ml. of boiling 50% sulfuric acid, and the furan steam-distilled to give 4 g. (40% based on the nitro compound) of material, m. p. 106-106.5° after recrystallization from ethanol.
- 3-Cyanocarbazole. (Example of preparation of a triazine and of a carbazole by thermal decomposition of the triazine.)<sup>103</sup> 2-Nitro-4-cyanodiphenylamine is prepared in 78% yield by heating to the boiling point equimolecular quantities of aniline and of 4-chloro-3-nitrobenzo-nitrile. Reduction in 78% yield is earried out with stannous chloride in glacial acetic acid and hydrochlorie acid. Diazotization yields the triazole in 65% yield. The triazole (1 g.) is heated in a metal bath until nitrogen evolution ceases. Extraction with ethanol and recrystallization from toluene gives 0.3 g. (35%) of 3-cyanocarbazole, m. p. 184–185°.

### TABULAR SURVEY OF DIAZONIUM RING CLOSURE REACTIONS

The various examples of the eyelization reaction have been grouped in the following tables according to the type of bridge group involved. The examples are intended to be complete through May, 1956, although by the very nature of the subject some references will certainly have been overlooked. Table IV, which lists a number of examples of earbazole derivatives that have been prepared by heating triazoles, does not aim at completeness.

<sup>103</sup> Preston, Tucker, and Cameron, J. Chem. Soc., 1942, 500.

Aq. C2H5OH, H2SO4, Cu Nitrosoamide, (C2H5)20 Nitrosoamide, CeH Dry, acetonc, Cu\* Dry, acctonc, Cu\*

Trlazenet

47 25 47 47 47 47 25 25 25 25 25

60 57 75 81 81 43 37 37 18

### TABLE I

# PHENANTHRENE DERIVATIVES

Product				/0 E1-17K	Defendance
Formula	Starting Amine	Product	Conditions	x icid, %	reference
	or of the confidence	Phenanthrene	Aq. H <sub>2</sub> SO <sub>4</sub>	16-42	35
C111110	Cls-2-A minicalineance		Aq. H.SO, Cu	08-09	32, 42
			C,H.OH, H,SO,, Cu	65	42
			Na.CO.	1	104
			Aq. H2SO4, NaH2PO2,	80	42
			Cu		
	cia. 9 1'. Maminost Mone	Phenanthrene	C,H,OH, H,SO,, Cu	18	105
C1,111,13r,02	C,11,11,18r,0, trans-2-Amino-4-bromo-a-(4'-bromophenyl)-	3,6-Dibromophenanthrene-9-carboxylic	Aq. C2H5OH, Na2CO3,	70-90 crude	106
	cinnamic acid	neid	Cu, NaH2PO2		
C1311,C1202	C13116Cl2O2 trans-2-Amino-a-(3',4'-dichlorophenyl)cinnamic	5,6- and 6.7-Dichlorophenanthrene-	Aq. C <sub>2</sub> H <sub>5</sub> OH, HCl, Cu,	75 crude	107
	uehl .	9-carboxylic acid	$NaH_2PO_2$		
C13II, 11rO2	trans-2-Amino-x-(2'-bromophenyl)elunamic acid	8-Bromophenanthrenc-9-carboxylic acid	C <sub>2</sub> H <sub>5</sub> OH, HCl, Cu	20-60	20
	trans-2-Amino-2-(1'-bromophenyi)clunamic acid	6-Bromophenanthrene-9-carboxylic acid	Aq. H2SO4	1	15, 108
C14114C103	-	2-Chlorophenanthrene-9-carboxylic acid	Aq. H2SO4, Cu	65	108
	_	3-Chlorophenanthrene-9-carboxylie aeld	Aq. C2HsOH, H2SO4, Cu	30	84
	frans-2-Amino-z-(4'-chiorophenyi)chmamic acid	6-Chlorophenanthrenc-9-carboxylic acid	Aq. H2SO,	28	109, 110
:			Aq. H2SO4, Cu	58	
Clyll,NO	3.(2' Iminobenzylidene) oxindole	Lactam of 8-aminophenanthrene-	Aq. H2SO4, Cu	75	15
:			•		
C18119	Cistle No. trans-2-Amino-a-(27-nitrophenyi)elnnamie acid	8-Nitrophenanthrene-9-carboxylle acid	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	24	111
5	the state of the s		Acetone, Cu	57	
A111110	citilions and contraction of the	Phenanthrene-O-carboxylle acid	Aq. H2SO4, Cu	93 crude	4, 25
			Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	98	1.5
			Aq. HCl, Cu bronze	40	25
			$Aq. H_2SO_4$	09	47
			Aq. $p$ H 5	57	25
			Aq. pH 7	75	47

trant-2-Amino-1-(4'-aminophanylleinnamie acid Phenanthrene-9-earboxylle aeld Nat. Beforences 104-225 are listed on pp. 450-462.

<sup>\*</sup> The crystalling diaxonium chiefile was used, and the yield is based on the diazonium saft, ! The telerene was obtained by coupling the diamonium salt with dimethylamine,

### TABLE I-Continued

## PHENANTHRENE DERIVATIVES

		PHENANTHICENE CONTROL		Violal 0%	Reference
•		Product	Conditions	11cm: //	
Product Formula	Starting Amine		Aq. NaOll	92	15
$C_{15}H_{10}O_{3}$	trans-2-Amino-5-hydroxy-a-phenylcinnamic	2-Hydroxyphenantincoch carbons 2-1	Aq. acld	40-45	15
$C_{16}H_8O_3$	acid trans-2-Amino-a-(2'-carboxyphenyl)cinnamic acid acid (4'-cyaoophenyl)cinnamic acid	ic acld eld	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	85	111
C16H9NO2 C16H10O4	trans-2-Amino-a-(4'-carboxyphenyi)cinnamic acid	Phenantinene C.3 area 2 3 Acethylene (10 x volenantirene 9 -	лд. С <sub>2</sub> 1150И, И <sub>2</sub> SO4. Сп	ig.	112, 113
$G_{16}H_{12}O_{2}$	trans-2-Amioo-4,5-methylenedioxy-α- pheoylennamic acid pheoylennamic acid trans-2-Amino-5-methyl-α-phenylennamic acid trans-2-Amino-3-methyl-α-phenylennamic acid		Aq. 115804 Aq. 115804 Aq. 115804. Cu	75 crude 75 crude 20	07 07 21
	trans-2-Amino-a-(4'-methylphenyl)cinnamic acid		Na,CO <sub>3</sub> HCi, C <sub>2</sub> H <sub>5</sub> OH, Cu	<u> </u>	0.5
	trans-a-(2'-Amiso-5'-methylphenyl)cinnamic acid 6-Methylphenanthrenc-9-carboxylic acid self self self self self self self self	<u> </u>	Aq. 11,80, Aq. 11,80, Cu Aq. 11,80, Cu	° 00-10	202
	trans-3-Methyl-a-(2'-aminophenyi)cinnanile acid	2- and 4-delity phononements acid acid 5- and 5-Methylphonanthrene-9-	Aq. 113.504	1	10
C14H12O3	trans-2-Amioo-a-(3'-methylphenyl)cinnanic acid trans-2-Amino-5-methoxy-a-phenylcinnamic acid	erboxylic acid 2-Methoxypicnanthrene-9-carboxylic neld 4-Methoxyphenanthrene-9-carboxylic acid	Na <sub>1</sub> CO <sub>3</sub> 11 <sub>5</sub> SO <sub>4</sub> Cu	80 Quant.	00 8 5
	trans-2-Amino-a-(4'-methoxyphenyl)clinianile trans-2-Amioo-a-(4'-methoxyphenyl)clinianile acid	6-Methoxyphenanthrene-9-carboxylle ackl 8-Yesthoxyphenanthrene-9-carboxylle ackl	112.504. Cil	22	••
	trans-2-Amino-\alpha-(2'-methoxyphenyt)einnanne aeid	3-1fydroxy-1-methoxyphenanthrene-	ու 504, Հո	ra. 3	
C16H12O4	trans-2-Amioo-3-methoxy-4-nymoxy-x- phenyicinnamic acid	9-earboxylle acid 4-Hydroxy-3-methoxyphenanthrene-	NaOH	60 crude	13
1	(rans-2-Amiso-3-hydroxy-4-methoxy- a-phenyleinnamic acid	9-carboxylle neld 8-Bromo-4-methoxy-5,6-methylenedloxy-	.м. си,оп, п, 804, Си	15	çi
C <sub>17</sub> H <sub>11</sub> BrO <sub>5</sub> C <sub>17</sub> H <sub>12</sub> O <sub>5</sub>		phenanthrene-9-carboxylic neith 4-Methoxy-6,7-methylenedloxyphenan- threne-9-carboxylic neid	H <sub>2</sub> SO <sub>1</sub> , Cu	1	ç1  -

0	$C_{17}H_{13}{ m BrO}_4$ trans-2-Amino-3,4-dimethoxy-6-bromo- $lpha$ -phenylchnamic acid	I-Bromo-3,4-dimethoxyphenanthrene- 9-carboxylic acid	Aq. C <sub>2</sub> H <sub>5</sub> OH, HCl. Cu	70-80	66
trans- α-p	trans-2-Amino-3,4-dimethoxy-5-bromo- a-phenyleinnamle acid	2-Bromo-3,4-dimethoxyphenanthrene- 9-carboxylic acid	С <sub>2</sub> П <sub>5</sub> ОН, НСІ, Си	95 crude	99
trans- pho	trans-2-Amino-3, 4-dimethoxy-a(2'-bromo- phenyl)cinnamic acid	8-Bromo-3,4-dimethoxyphenanthrene- 9-carboxylie acid	.Мq. С <sub>2</sub> Н <sub>5</sub> ОН, НСІ, Сu	09	1.5
trans- phe	!rans-2-Amino-a-(2'-bromo-4',5'-dlmethoxy- phenyl)clinnamic acid	8-Bromo-5, 6-dimethoxyphenanthrene- 9-carboxylle acid	Aη. H <sub>2</sub> SO <sub>4</sub> , Cu	60-65	19, 99
trans-	$lrans-2-Amino-4,5-dimethoxy-\alpha-(4'-chioro-plicny])$ cinnamle acid	6-Chloro-2,3-dimethoxyphenanthrene- 9-carboxylle acid	$Aq. C_2H_5OH, H_2SO_4, Cu$	35	115
trans cin	trans-2-Amino-3-methyl- $\alpha$ -(4'-methylphicnyl)- cinnamic acid	4,6-Dimethylphenanthrene-9-carboxylic acid	Aq. C <sub>2</sub> H <sub>5</sub> OH, HCl, Cu,	11	73
trans- cin	trans-2-Amino-æ-(2',5'-dimethylphenyl). einnamle aeld	5,8-Dimethylphenanthrene-9-carboxylic acid	A4. C2H5OH, HCl, Cu	85 crude	116
<i>tran</i> s cir	trans-2-Amino-a-(2',4'-dimethylphenyl). cinnamic acid	6,8-Dimethylphenanthrene-9-carboxylic	Ач. С <sub>2</sub> Н <sub>5</sub> ОП, НСІ, Си	87 crude	83
trans	trans-2-Amino-a-(3'-cthylphenyl)chnamic acid	5- and 7-Ethylphenanthrene-9-carboxylic	H <sub>2</sub> SO <sub>4</sub> , Cu	95	117
tran	trans-2-Amino-a-(4'-ethylplıcnyl)clnnamic acid	6-Ethylphenanthrene-9-carboxylle aeld	Aq. H,SO., Cu	Ģ	ć
tran	trans-2-Amino-3-methoxy-a-(2'-methylphenyl)- clanamic acid	4-Methoxy-8-methylphenanthrene- 9-carboxylle acid	Аq. С <mark>2</mark> Н <sub>5</sub> О́И, НСІ, Сu NaOH	80 crude 43	118
cl	clanamic acid		$\mathrm{CH_3OH},\mathrm{II_2SO_4}$	1	119
cl tran	cinnamic acid cinnamic acid trans-2-Amino-a-(2', methous, 2		МаОН	1	120
ci tran	cinnamic acid  Crans-2-Amino-a-(4'-cthownshimmic acid		Na <sub>2</sub> CO <sub>3</sub> , Cu	1	62
trans	trans-2-Amino-4,5-dimethoxy-a-phenyl-	1 6-Ethoxyphenauthrene-9-carboxylic acid 2,3-Dimethoxyphenauthrene-9-carboxylic acid	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	50-60	114
cin (rans-	cinnamic acid	3,4-Dimethoxyphenanthrene-9-carboxylic acid	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	70-80	) e
clnnc	cinnamic acid trans-2-Anino-5-methoxy-a-(3'-methoxy-	6,7-Dimethoxyphenanthrenc-9-carboxylic acid	Aq. H <sub>2</sub> SO <sub>4</sub>	09	121, 122 19
cinna	cinnamic acid	2,5-Dimethoxyphenanthrene-9-carboxylic acid	Aq. Na <sub>2</sub> CO <sub>3</sub>	35	123
гепсев	Note: References 104-225 are listed on pp. 460-462.	2,7-Dimethoxyphenanthrenę-9-carboxylle acid		88	ì

## TABLE I-Continued Phenanthrens Derivatives

The Germanich	Nelection:	11	·s	<u>\$</u>	5	3	521	125		2	ä	53	20, 127	n	**
	Yleid, 75	9.	55-05	12	so crade	1	i	ì		:	i	ł	15-50	<b>5</b>	oç O
	Conditions	.л. кон	Aq. 112804. Cu	Aq. 11380.	Ag. C <sub>2</sub> 115011, 11Cl. Cu	ì	1	;		;	:	A4. 11,50,	Ad. Wash, Co	Aq. C. 11,011, 1101, Ca.	Nall <sub>3</sub> PO <sub>3</sub> No. C <sub>4</sub> ll <sub>4</sub> Oll, 11°1, Cu. Sall <sub>3</sub> PO <sub>3</sub>
PHENANTHRENE DERIVATIVES	#online#	*5125241444444	3,6-Dimethoxy-1-liydroxylylenantur. 9-carboxylle acid	4.3. Dimethoxys-3-fly moves from the first of the first o	Spelleathory lie ach	threne-9-carbovylle acid	dloxyphenauthrene-9-earloxy Be acid	dloxythenathene-9-cathoxytle acht acht acht acht acht achtenene	threne-g-carboxylic acts and 1,2. dimethoxy-5,6-methylene-floxy-	phenanthrene-deathory is a con- 2,7-Dimethoxy-6,7-methylenedloxy plenan- threne-9-earboxy lie acid and 2,7-di-	methoxy-5, 6-methylenedievy- phenanthrene-9-earl-oxy lie aeld	3.4-Dimeticety-6,-membrossor phenanthrate-9-carloxylle acid 5-Hromo-3.4,-trimethoxygd-caatthrass	g-carboxylic acld 4-Bromo-3, 1.5-trimethoxy phenylthrene-	9-earhoxylle acid	9-carboxylle ach 7-Ethyl-1-methylphenanthrene- 9-carboxylle ach
		Starting Anine	trans-2-Amino-3-hydroxy-4-methoxy-2-(4'-	trans-2-Amino-3-methoxy-4-hydroxy-z-(2*- methoxyphenyl)chnamic acld	trans-2-Amioo-3, 4-dimethoxy-x-(2'-carboxy-	trans-2-Amino-4,5-methylenedloxy-2-(2'.5'- dimethylphenylychnamic acid	C19H13BrO6 trans-2. Amino-5, G-dimethoxy-2-(2'-bromo-1',5'-mino-6, G-dimethoxy) methylenedioxyinenyl) elimamic acid	trans.2.1mino-4,5-dimethoxy-x-(2'.bronio-1'.a'- inethylenedioxyphenyl)cinnamic acid	trans-2-Amino-5,6-dimethoxy-x-(3',1'- incthylenedioxyphenyl)chnamic acid	trans-2-Amino-4,5-dimethoxy-2-(3',4'-		trans-2-Amino-3, t-dimethoxy-2-(3', 1'- methylenedloxyphenyl)clinnamic acid	C14H15BrO, trans-2-Amino-3, I-dinetioxy-zvo-recon-z- metioxyphenylchnamic acid metioxyphenylchnamic acid	trans-2-Amino-3,4-dinetioxy-2-1,2-months methoxyphenyl)cinoamie acid	trans-2-Amino-3-methyl-2-(4-ethylphenyl)- chnamic acid trans-2-Amino-3-methyl-2-(3'-ethylphenyl)- chnamic acid
	1	Formula	C17H14O3		$c_{18}H_{12}O_{5}$	$C_{18}H_{14}O_4$	$c_{19} \pi_{13} \mathrm{BrO}_6$		C14H14O6				C <sub>14</sub> III <sub>15</sub> BrO <sub>1</sub>		CIAH 1402

137 138

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Aq. dioxane, NaH<sub>2</sub>PO<sub>2</sub>, Cu, H<sub>2</sub>SO<sub>4</sub> Aq. Na<sub>2</sub>CO<sub>3</sub>

9-carboxylic aeld

15	15	128	12	16	20	76, 129, 130	74, 130	131, 132	133a	83	133b	128	134	11	135, 136	137
80	90 erude	47 crude	20	1	i	9	9.0 8.0 9.0	27	30	65 crudo	61	20	83 crude	80	20	63
Αη. C <sub>2</sub> H <sub>5</sub> OH, HCl, Cu	Aq. Na <sub>2</sub> CO <sub>3</sub>	Dioxane, H <sub>2</sub> SO <sub>4</sub> , Cu, NaH,PO,	Aq. H <sub>2</sub> SO <sub>4</sub>	Aq. C <sub>2</sub> H <sub>5</sub> OH, HCl, Cu	Aq. CH3OH, H2SO4	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	Aq. C2H5OH, H2SO4, C11,	NaH <sub>2</sub> PO <sub>2</sub> Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	Aq. C <sub>2</sub> H <sub>5</sub> OH, HCl, Cu	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	Dloxane, H2SO4,	Dloxane, H <sub>2</sub> SO <sub>4</sub> ,	Aq. CH30H, H2SO4	Aq. $\mathrm{H}_2\mathrm{SO}_4$	Aq. dioxane, NaH, PO.,
3,4-Dimethoxy-6-methylphenanthrene- 9-earboxylle aeld	3,4.Dimethoxy-8-methylphenanthrene- 9-carboxylle aeld	5,8-Dimethyl-3-hydroxy-4-methoxy-phenanthrenc-9-carboxylic acid	3,4,6-Trimethoxyphenanthrene- 9-oarboxylic acid	3.4.8-Trimethoxyphenanthrenc-9-carboxylic Aq. C <sub>2</sub> H <sub>5</sub> OH, HCl, Cu acid	3,4,5- and 3,4,7-Trimethoxyphenanthrene- 9-carboxylic acld	Benzofelphenauthrene-6-carboxylic acid	Chrysene-5-carboxylic acid	NaH <sub>2</sub> PO <sub>2</sub> 8-Bromo-3,4,5,6-tetramethoxyphenanthrene- Aq. H <sub>2</sub> SO <sub>4</sub> , Cu 9-earboxylic acid	5,6,7,8-Tetramethylphenanthrene- 9-carboxyllc acid	8-Methyl-5-lsopropylphenanthrene- 9-carboxylle acld	6-Isopropyl-8-methylphenanthrene- 9-carboxylle acid	3,4.Dlmethoxy.5,8.dimethyiphenanthrene- 9-earboxylic acid	2,3-Dimethoxy-5,8-dimethylphenanthrene- 9-earboxylic aeld	8-Ethoxy-3,4-dimethoxyphenanthrene- 9-carboxyllc acid		2,5,6,7-Tetramethoxyphenanthrene-
trans-2-Andon-3,4-dimethoxy- $\alpha$ -(4'-methyl-phenyl)elnnamie acld	trans-2-Amino-3,4-dimethoxy-α-(2'-methyi- phenyl)cinnamic acid	trans-2-Amino-4-hydroxy-3-methoxy-\alpha(2',5'-dimethylphenyl)einnamic acid	trans-2-Amino-3,4-dimethoxy-α-(4'-methoxy- phenyl)chnamic aeld	trans-2-Amino-3,4-dimethoxy-α-(2'-methoxy-picnyl)chnamie acid	trans-2-Amino-3,4-dlmethoxy-\alpha-(3'-methoxy-phenyl)clmnamle acld	<i>trans-2-A</i> mlnο-α-(2'-naphthyl)einnamie acid	trans-2-Amino-a-(1'-naphthyl)cinnamic aeld	C191117 BrO traus-2-Amho-3,4-dimethoxy-a-(2'-hromo-4',5'-dimethoxyphenyl)chnamie aeld	clunanle acid	chnamic acid	clinanic acid	dimethylphenylelmamle aeld				phenyl)cinnamie acid
C16 H16 O4		:	C18H16O5		;	C18 II 12 O2		CisHrBro	C1811803		C,M,		CisH 18Os	CisH <sub>16</sub> O <sub>8</sub>		

Note: References 104-225 are listed on pp. 460-462.

# TABLE I—Continued

VATIVES
в Dекг
NTHREN
PHENA

Reference	139	18	140	136	131, 132		141	81	143	143		143		144	145	146
Yicid, %	50 ernde	30	65	I	9	13	95 erude	22	32	35	13	35	6	10	30	65 crude
Conditions	0°4	Aq. CII3OH, H2SO4	Dimethylformamide,	H <sub>2</sub> SO <sub>4</sub> , Cu λη, Να <sub>2</sub> CO <sub>3</sub>	Aq, H2SO4, Cu		Aq, dioxane, C2H5OH,	п <sub>2</sub> SO <sub>4</sub> , Сп, NaH <sub>2</sub> PO <sub>2</sub> Aq, С <sub>2</sub> H <sub>5</sub> OH, Na <sub>2</sub> CO <sub>3</sub>	Aq. CII,0H, II <sub>2</sub> SO <sub>4</sub>	Aq. CH3OH, H2SO4, Cu Aq. CH3OH, H2SO4, Cu		Aq. CH3OH, H2SO4, Cu		Dioxane, C2H3OH, Cu.	NaH <sub>2</sub> PO <sub>2</sub> Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	Aq. (lso $C_5H_{11}$ ) $_2$ O, $H_2$ SO $_4$ , $C_{10}$ , Na $H_2$ PO $_2$
PHENANTHRENE LEMANT	Product	3,4,5,8-Tetranethoxyphic	3,4,6,8-Tetramethoxyphenancae 9-earboxylic aeld	2,3,4,7-Tetramethoxyphenantuncuc g-carboxylle aeld	2,3,4,5- and 2,3,4,7-remained phenanthrene-9-carboxylic acid	3,4,5,6-fettameeners) menses 9-carboxylic acld	3,4,0,7-1ettaneciacy	8,0-Methylenedloxyentysene 5-earboxylle aeld	į	5-Ediyi-3,4,8-trimethoxyphenanteners 9-earboxylic acid	9-earboxylic acid 9-earboxylic acid 7 75-6000 3 4 5-frimethoxyphenanthrene	o-Euloxy-3,4,5 g-carboxylic acid 7-Ethoxy-3,4,6-trinethoxyphenanthrene-	9-carboxylic acid 5-Ethoxy-3, 4, 6-trimethoxyphenanthrene-	grantony or to and grantony is acid	Cholantin energy company of 19. Dimethylehrysene-5-earboxylic acld	1,2-Dimethoxyclirysene-6-carboxylle aeld
	Starting Amine	trans-2-Amino-3,4-dimethoxy-a-(2',5'-	dimethoxyphenylleminess.  trans-2-Amino-3,4-dimethoxy-a-(2,4'-	dincthoxyphenyllenmanne eel. trans-3,4,5-Trimethoxy-a-(2'-amino-5'-	methoxy prices from the process. A mino-3, 4,5-trimethoxy-\alpha-(3'-nicthoxy-\alpha-1) mino-3, 4,5-trimethoxy-\alpha-(3'-nicthoxy-\alpha-1) manie acid	prens, y, rans-2, Anino-3, 4-di methoxy-α-(3', 4'-		trans-2-Amino-4,5-methylenedioxy-a-	trans-2-Amino-5-methoxy-a-(1'-naphthyl)-	cinnamic acia l/αns.2-Amino-3,4-dinicthoxy-α-(5'-ethyl- o'-methoxyphenyl)cinnamie acid	trans-2-Amino-3,4-dimethoxy-a-(4'-ethoxy-3',-m-thoxy)	and H. Jos	trans-2-Amino-3,4-dimethoxy-α-(3-emoxy- 4'-methoxyphenyl)cinnamic acid		trans-2-Amino-a-(3'-acenaphthenyl)clinamie aeld	trans-2-Amino-a-(3',4'-dlmethyl-1'-naphthyl)- einnamie acid trans-2-Amino-3,4-dlmethoxy-a-(1'-naphthyl)- einnamic acid
	Product Formula	C, II, O	(Cont.)					$C_{20}\Pi_{12}O_4$	C20II1403	C20H20Os	$\mathrm{C}_{20}\mathrm{H}_{20}\mathrm{O}_6$				$\mathrm{C}_{21}\mathrm{H}_{14}\mathrm{O}_{2}$	C21H16O2

### LABLE II

DIHYDROPHENANTHRENE DERIVATIVES

Doforono	Yleid, % meretare	25	25	52	<b>2</b>	4, 86	98	86		96		156		81			
/0	Y leiu, %	4	40	0	20	l	l	20		15		Small		45	None		
	Conditions	CII CO TI CO	Aq. dioxane, 1122 o4; c.	OF THE OPENING	Triazene SO. Cu			Aq. H2504, Cu	A4. 1125041 C.	An H.SO., Ch	الماراء بدقت في	An H.SO. Cu	in all the state of the state o	te dievane HCl. Cu	At CO Or CH. CO.Na	1812CO3 OF CE3CC2	
Ulliamorate	Product		a c. Dibydrobenzoff]quinoline	200		o 10. Dihydronhenanthrene	2, to Thurstonhenanthrene-9-carboxylle acid	o 10. Dilydrophenanthrene-9-earboxylic acid	9 30r 3 4-)-Methylenedioxy-9,10-dihydrop-	henanthrene-9-carboxylle aeld	a.Methoxv-9,10-dlhydrophenanthrene-	9-carboxylie aeld	10-Methyl-9,10-dihydrophenanthrener	9-earboxylie acid	9.3.4.7-Tetramethoxy-9-cyann-9,10-dinydro-	phenanthrene	
MINICI TO THE PROPERTY OF THE		Starting Amine			(			acid	~.(2.Aminophenyl)-\theta-phenyl)proplonie acid	α.(2-Aminophenyi)-β.(3',4'-methylenedioxy-	phenyl)propionic acid	\alpha \cdot (2. Antinophenyl) \beta \cdot (4' -methoxy phenyl) \partial \cdot (4' -methoxy phenyl) \partial \cdot (4' -methoxy phenyl)  \text{9-carboxy lie aeld}	aeid in the said	$\alpha$ -(2-Aminophenyl)- $\beta$ -phenylbutyric acm		. 6, 4, 3	trimethoxyphenyl)propionitriic
	to the state of	Pormula		;	C13 II N			C14112		0.11.0		C110,				C.H.sNO,	5 . sl . sl .

Note: References 104-225 are listed on pp. 460-462.
• The triazenc was prepared by coupling the diazonium salt with dimethylamine and was then heated in henzene solution while hydrogen chloride was bubbled In.

### TABLE III

# FLUORANTHENE DERIVATIVES

Numbering System for Fluoranthene

		Yield, % Reference	ç	88, 157	157	88	158	158	158	159	7.7	88	160	161	162	162
		Yield, %	43	ı	÷;;	i	1	œ.	1	55	Poor	15	1	38	1	1
) =		Conditions	An. CH3CO2H, H3SO4, Ch	Aq. H <sub>2</sub> SO <sub>1</sub> , Cu	Ad. CH3CO2II, H2SO,	Ad. 11 20 Cil	Ad. maso, ca	Ad: 113:504, Cli	Ad. Chiscosil, Hiso, Cu	Aq. 11(1, Ca	Aq. 112504, Cu	Aq. 11250, Cu	Aq. 112504. Cu	Aq. Clistozii, H.so. Cu	Ad. CH3CO2H, H2SO4, Cu	At. CHICOLII. HESOL, Cu
)  -	Product	ī	rivoranthene 7-Nethylfuoranthene													
	Starting Amine	1-(2'-Aminophenyl)naplithalene	1-(2"-Amino-6'-methylphenyl)naphthalene 1-(2"-Amino-3'-methylphenyl)naphthalene	1-(2'-Amino-4'-methylphenylpashensian	1-(2'-Aminophenyl)-2-methoxynanhthalene	1-(2'-Aminophenyl)-4-methoxynaphthalene	1-(2'-Methoxyphenyl)-8-aminonanlithalane	1-(2'-Amino-4'-methoxyphenyhnanhthalan	1.(2Aminophenyl)-2,4-dimethylnanhthalan	1-(2'-Amino-4'-earbethoxyphenylmanhthaten	1-(2'-Aminophenyl)-2,3,4-trimethylnamhthalan	3-(2'-Aminophenyl)fluoranthene	4-(Z-Anihophenyl)-1-methylfluoranthene	4-(2'-Aminophenyl)-2-methylfluoranthene	eferences 104-995 one items	The use of copper did not increase the viers
Product	Formula	CleH <sub>10</sub>			$C_{17}II_{12}O$							C-H			Note: Re	* The use of eoppe

Note: References 104-225 are listed on pp. 460-462.
\* The use of copper did not increase the yield.

### TABLE IV

CARBAZOLE DERIVATIVES PREPARED VIA TRIAZOLES

Numbering System for Carbazole

12 0 60 10 10 10	The second second	165	164	164	169	168	168	170 171	172 173	
Product	Name		1,3-Dimethylcarbazolc 8,10-Dinitro-7-benz[kl]aeridine	Benzo[a]carbazolc 7-Benz[kl]acrldine	10-Methylbenzo[e]earbazole	3-18enzoy een ververe 7-Bromo-12-naphtho[2,3-a]earbazole-5,13-dlone	12-Naphtho[2,3-a]carbazolc-5,13-dione	1,1'-Bicarbazole	3,3'-Bicarbazone	3,6-Dipenzoy/Karroazoa
P4	Formula		CHINAN	CleHilN	C <sub>17</sub> II <sub>13</sub> N	$c_{19}H_{13}NO$ $c_{20}H_{19}BrNO_{3}$	$c_{20}H_{11}NO_2$	C21H16N2		$c_{26}H_{17}NO_2$
	TheConomic	Meterores	163	105	163	165	103 103 69, 167	103	105 163	103
	Product	Name	5-Pyrid[4,3-b]indole	1,3-Dinitrocarbazole 2-Chlorocarbazole	3-Chlorocarbazole	3-Aminocarbazole	1.Nitrocarbazole 3.Nitrocarbazole	Carbazole 3-Cyanocarbazole	1-Methylearbazole 3-Methylearbazole 7 Amethylearbazole	3-Acetylcarbazole
		Pormula	C. 11. N.	O.N. 11.17	- Internation	C1111,N1	C12 JI 4 N 2 O 2	C <sub>13</sub> H <sub>2</sub> N N <sub>2</sub> H <sub>2</sub> N	C <sub>13</sub> H <sub>11</sub> N	C111112N1 C111111N0

Note: References 104-225 are listed on pp. 460-462.

### TABLE VI

# Dimensioperany Derivatives and Scheue Analogs

Numbering System for Dibenzefuran

Yield, % Reference	571 571 571	176 176 176	871 871 771	176 178 30 30
Yleld, %	111	1111	110	18500
Procedure	. Aq. 11 <sub>2</sub> 504 . Aq. 11 <sub>2</sub> 504	. 11, 11, 12, 13, 14, 11, 15, 15, 14, 17, 15, 15, 14, 17, 17, 17, 17, 17, 17, 17, 17, 17, 17	Aq. 112504 Aq. 112504 Aq. 112504 Aq. 112504	Aq. II <sub>2</sub> SO <sub>4</sub> Aq. II <sub>2</sub> SO <sub>4</sub> Aq. II <sub>2</sub> SO <sub>4</sub> Aq. XaOII + CuOII Aq. XaOII
Product	2,7. Dibromedibenzofuran 2,8. Dibromedibenzofuran	2-Chloro-7-altrodlbenzofuran 2,5-Dichloradlbenzofuran 2-Bromodlbenzofuran 2-Bromodlbenzofuran	3-UromodDenzofuran 2-ChlorodDenzofuran 2-ChlorodDenzofuran 3-ChlorodDenzofuran	3-Niroalibenzofaran Dibenzofaran
Statiba, Malerial	Call, Brgo 2-Ambre Caditremediphenyl ether	C <sub>1</sub> H <sub>2</sub> C(N) <sub>2</sub> 2-Audios C-disres-Sultrodiphenyl ether C <sub>1</sub> H <sub>3</sub> C(1) <sub>2</sub> 2-Audios (1-dichlorodiphenyl ether C <sub>1</sub> H <sub>3</sub> C(1) <sub>3</sub> 2-Audios (4-Aramodiphenyl ether C <sub>1</sub> H <sub>3</sub> Hatt (1-2) <sub>3</sub> Audios (4-Aramodiphenyl ether	2. Amino-5-bronnedlighenyl ether 2. Amino-1-chloredlighenyl ether 2. Amino-Y-chloredlighenyl ether 3. Amino-Y-chloredlighenyl ether	2.Amino-5-morompieny ether 2.Amino-5-mittodipieny ether 2.Amino-lipieny ether
Profess	C,111,13r,0	Cancolor Cancolor Cancolor	Chillicio	0,111,201 0,111,301

102 102 58 179 46 30 30	8 8 8 8	180 30 30	30 30 181 180	180 180 182
15 40 20 40 40 15 25–35	5 <30 None	22 22 23-10	None 3 70 32	Trace 0
Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub>	11,504, CuSO4, UNOOH	HOI, OH 85%, H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>3</sub> SO <sub>4</sub> , Cu	Aq. NaOH Aq. H <sub>2</sub> SQ <sub>4</sub> , Cu Aq. CH <sub>3</sub> CO <sub>2</sub> H, HCl, Cu Aq. CH <sub>3</sub> CO <sub>2</sub> H, HCl, Cu	П <sub>2</sub> SO <sub>4</sub> Ач. СН <sub>3</sub> CO <sub>2</sub> H, ПСІ, Си Аq. СН <sub>3</sub> COOH, ПСІ, Си 50% H <sub>2</sub> SO <sub>4</sub>
2-Bromodlbenzofuran-6-earboxylle acid 2-Bromo-4-methyldlbenzofuran 2-Bromo-8-methoxydlbenzofuran 2-Nitrodihenzothlophene Dibenzothlophene	Dibenzothiophene dioxide	Dibenzoselenophene 2-Methyldibenzothlophene	2-Nethyldlbenzothiophene dioxide 2-Ethoxy-8-nitrodlbenzothlophene Naphtho(1,2-b)thlanaphthene-11-dloxido	Naphtho(2,1-b)thlanaphthene-7-dloxido Naphtho(1,2-b)thlanaphthene Naphtho(2,1-b)thlanaphthene
2-Amino-4'-bromo-G-earboxydiphenyl ether 2-Amino-4-bromo-6-methyldiphenyl ether 2-Amino-4-bromo-4'-methoxydiphenyl ether 2-Amino-4-nitrodiphenyl sulfido 2-Aminodiphenyl sulfide	2-Aminodiphenyi sulfone	2-Aminodiphenyl selenido 2-Amino-4'-methyldiphenyl sulfide	G <sub>13</sub> H <sub>10</sub> O <sub>2</sub> S 2-Amino-4'-methyidiphenyi sulfono G <sub>14</sub> H <sub>11</sub> NO <sub>3</sub> S 2-Amino-4-nitro-4'-ethoxydiphenyi sulfide G <sub>14</sub> H <sub>10</sub> O <sub>2</sub> S 2-Aminophenyi-1'-napithyi sulfone	2-Aminophenyl-2'-naphthyl suifone 2-Amino-2-naphthyl suifide 1-Amino-2-naphthyl phenyl suifide Note: References 104-225 are listed on pp. 460-462.
C <sub>13</sub> H, <sup>3</sup> DrO <sub>3</sub> C <sub>13</sub> H, <sup>3</sup> DrO <sub>2</sub> C <sub>12</sub> H, <sup>3</sup> DrO <sub>2</sub> C <sub>12</sub> H, <sup>3</sup> NO <sub>2</sub> S C <sub>12</sub> H <sub>8</sub> S	C <sub>12</sub> H <sub>8</sub> O <sub>2</sub> S	C <sub>12</sub> H <sub>4</sub> Se C <sub>13</sub> H <sub>10</sub> S	C <sub>13</sub> H <sub>10</sub> O <sub>2</sub> S C <sub>14</sub> H <sub>11</sub> NO C <sub>16</sub> H <sub>10</sub> O <sub>2</sub>	C <sub>16</sub> H <sub>10</sub> S

TABLE VII

Fromus Demyataus

Reference	<b>777</b>	1 47 183	183	183	181	183
Yleld, %	E 0 0 0	o	16	81	30	1
Procedure	Aq. 11Cl Aq. HCl. Cu (C <sub>4</sub> U <sub>5</sub> ) <sub>2</sub> O. Cu Acetone, Cu	.Nq. II <sub>2</sub> SO <sub>4</sub> Nitrosanido, C <sub>6</sub> II <sub>6</sub> .Nq. II <sub>2</sub> SO <sub>4</sub>	Aq. II <sub>2</sub> SO <sub>4</sub>	M. H2504	70% II SO.	ла. II <sub>3</sub> SO <sub>4</sub>
Product	Flustene	3, f : 10 - (dinethylamino) - 7 - nitro - 9 - phenyl-		**	g-phenylthorene 3,7,1'-Trl-(almethylamino)-0-phenylthorene	S. f131-(allmethylamino)-11-phenylbenzofal- luorene
statting Amine	N. Vertheallthan	and the standard and and the standards	heet ametay mingen of Santophenyl in the Calmethy landachtenyl in the Calmethyl i	ricitiane [14-(1'-direth)lamfnopheny D.2-amlno-	3-inethylphenylmethane 1(5-(1'-dinethylaminophenyl)=2-amino-	t-Jusethylaninophenylmethane 10.s.(V-dimethylaninophenyl)-2-amino- 1-asphthylmethano
	figlin.	: :	rannako,	7 Hand 1	C. H. N.	CrilleN

N.te; References 104-225 are listed on pp. 460-462.

### TABLE VIII

DERIVATIVES
FLUORENONE

Produet Formula	Starting Amlne	Product	Procedure	Yield, %	Reference
C <sub>13</sub> H <sub>6</sub> N <sub>2</sub> O <sub>5</sub>	•	2,4-Dinitrofluorenone	Aq. H <sub>2</sub> SO <sub>4</sub>	78 erude 25	185 186
13H, BrO	2-Amino-6-bromopenzopnenoue	1-blomuntande	Aq. H.SO.	2	100
13117NO3		1-Nitrofluorenone	Aq. H,50,	G	47
	z-Ammora -moreuzopnemone		Aq. H.SO4, Cu	2	47
			Acetone, Cu	0	47
	2-Amino-5-nitrobenzophenone	2-Nitrofluorenone	Aq. H,SO	55-60	100, 187
	•		Aq. H2SO4, Cu	45	
	2-Amino-4-nitrobenzophenone	3-Nitrofluorenone	Aq. CH,CO,Na, Cu	95 crude	100
	2-Amino-3-nitrobenzophenone	4-Nitrofluorenone	Aq. H,SO,	48	100
	2-Amino-3'-nitrobenzophenone	2-Nitrofluorenone	Aq. H2SO,	<sub>20</sub> *	31
1		4-Nitrofluorenone	1	15*	
C11HBO	2-Antinobenzophenone	Fluorenone	Aq. 112804	65*	31
			Aq. HASO4, CuSO4	*09	31
			Aq. H2SO4, Cu	71*	31
			pH 9, 12	25*	31
			Acetone, Cu	0	1-4
			Aq. HCl, H <sub>3</sub> PO <sub>2</sub> , Cu	0	24
			$NH_4OH + Cu$	10	30
			NaOH	20	31, 47
CHINN, OS	2.1 2.1 mino-6-methyl-3,5-dinitrobenzonhenone	1-Mother of dinte-du	$Aq. H_2SO_4$	80	95
:	2-Amino-4-methyl-3,5-dinitrobenzophenone	3.Methyl-9 4-dinitronuorenone	$Aq. H_2SO_4$	65	188
$C_{14}H_6O_3$		Fluorene-1-carboxylic acid	Aq. H <sub>2</sub> SO <sub>4</sub>	20	188
		Fluorene	$Aq. H_2 SO_4$	10	61
37.54	Media Dickers			10	
	Colorono of the color and the color of the colors of				

Note: References 104-225 are listed on pp. 460-462. • These yields are based on the isolated diazonium fluoborate; the other yields in the table are based on the amine.

# TABLE VIII-Continued

# FLUORENONE DERIVATIVES

Product	Product Permula Fermula  C <sub>11</sub> II <sub>2</sub> NO <sub>2</sub> 2-Amino-6-methyl-3-oltrobenzophenone 2-Amino-1-methyl-5-nitrobenzophenone 2-Amino-1-methyl-5-nitrobenzophenone 2-Amino-1-methyl-benzophenone 2-Amino-1-methyl-benzophenone 2-Amino-1-methyl-benzophenone 2-Amino-1-methyl-benzophenone 2-Amino-1-methyl-benzophenone 2-Amino-1-methyl-benzophenone 3-Methylituoren 2-Amino-1-methyl-benzophenone 3-Methylituoren 2-Amino-1-dellmethyl-5-nitrobenzophenone 3-Methylituoren 3-Methylitu				Procedure	Yield, % Reference	eferenco
Starting Annine demethyles a starting Annine demethyles a starting Annine demethyles a starting Annine demethyles a starting Annine demethyles a starting Annine demethyles a starting Annine demethyles and a starting Annine demethyles and a starting Annine demethyles and a starting Annine demethyles and a starting Annine demethyles and a starting Annine demethyles and a starting a starting and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting annine demethyles and a starting and a start	e _ n	durt		Product		;	100
2-Amino-t-methyl-5-pitrobenzophenone 3-Methyl-2-nitrofluorenone An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub> SO <sub>4</sub> 75 erude 50 An H <sub>3</sub>		nula	Starting Author		Art. II, SO4	99	180
1.4.   1.4.			ning. 6. wethyl.3.pitrobenzophenone	1.Methyl-f-nitronnorenone	Aq. H, SO.	75 ernde	180
2.Amino-3methylbenzophenone			nino-t-methyl-5-nitrobenzophenone	3-Methyl-7-nitrofluorenone	Aq. HCl	50	75, 102
2-Amino-4-nethylbenzophenone			nino-1-methylbenzophenone	1-Methylfinotenono 2-Methylfinotenono	Ag. HCl Ag. H <sub>2</sub> SO <sub>4</sub>	*09 *09	31, 187, 189
2.\text{Amino-4.'dulmethyl-3ultrobenzoplemone} 1.6-Dimethyl-4-nitrofluorenone	•		nings tomethylbenzophenone	3-Methyllinorenous 3-Methoxyfliorenono	Ad. H.SO.	55	188
9.Aurino-4,4"-dimethylbenzophenone         1,3"-Dimethylduorenone         Ad. H.\$O.         Cu         56           9.Aurino-2,1"-dimethylbenzophenone         1,4"-Dimethylduorenone			ning 4', methoxypenzopnenoue ning 4', 6-dimethyl-3-nitrobenzoplienone	1,6-Dinethyl-4-nitrofluorenone 3,6-Dimethyl-2-nitroflunrenone	Ad. HaSO.	8 C	191
2.\text{Amino-2.}; -\text{sulrequisement} = \frac{1.4.\text{Dinactlyylluocenone}}{1.4.\text{Dinactlyylluocenone}} = \frac{1.4.\text{Dinactlyylluocenone}}{1.4.\text{Dinactlyylluocenone}} = \frac{1.4.\text{Dinactlyylluocenone}}{1.6.\text{Dinactlyylluocenone}} = \frac{1.4.\text{Dinactlyylluocenone}}{1.6.\text{Dinactlyylluocenone}} = \frac{1.4.\text{Dinactlyylluocenone}}{1.6.\text{Dinactlyylluocenone}} = \frac{1.4.\text{Dinactlyylluocenone}}{1.6.\text{Dinactlyylluocenone}} = \frac{1.4.\text{Dinactlyylluocenone}}{1.6.\text{Dinactlyylluocenone}} = \frac{1.6.\text{Dinactlyylluocenone}}{1.6.\text{Dinactlyylluocenone}} = \frac{1.6.\text{Dinactlyylluocenone}}{1.6.\text{Dinactlyylluocenone}} = \frac{1.6.\text{Dinactly}}{1.6.\text{Dinactlyylluocenone}} = \frac{1.6.\text{Dinactlyylluocenone}}{1.6.\text{Dinactlyylluocenone}}			itno-4,4'-dhnethyl-5-nitrobenzopiwnowe	1,3.Dimethylfluorenono	Aq. II.504, Cu	20 V	<u> </u>
2-Aminn-5.2"-dimethy/thenzophenone 2,3-Dimethy/fithorenone Ad. H2SQ, Cu. Ad. H2SQ, Cu. Ad.			Almo-2',5'-dimethylbenzophenone	1,4-Dimethylituofenone 1 7-Dimethylituofenone	Ad. H.30.	86 20 20 20 20 20 20 20 20 20 20 20 20 20	101
2.Annino-3, 4dimethaxybenzophenone 2.3-Dimethoxylinorenone 2.4.Annino-3, 4dimethaxybenzophenone 2.3-Dimethoxylinorenone 2.4.Annino-3, 4dimethaxybenzophenone 2.3-Dimethoxylinorenone 2.4.Annino-3, 4dimethaxybenzophenone 2.3-Dimethoxylinorenone 2.4.Annino-3, 4dimethaxybenzophenone 2.4Dimethylianine 1.1-Chrysofluorenone 1.1-Chrysofluo		17.5 1.74	ninn-5,2*-dimethylbenzophenone	3,6.Dimethylduorenono	Aq. HCl	1	103
2.Antho.3.4'-dimethaxybenzaphenous 11-Chrysoftworenone 11-Chrysoft		•	tho-4,5-dimethnxybenzophenone	2,3.Dimethoxynnorenone o 3.Dimethoxynnorenone	Aq. II.SO.	60 erude 33	101
1-therapy1-2-implititylatinine 11-Chrysofluorenone 1.0-Xiv. 20. 13  1-(2-Anihobenzoyl)naphthilane 11-Benzofelfiluoren-7-none 7-Benzofelfiluoren-7-none 7-Benzofelfiluoren-7-none 7-Benzofelfiluoren-7-none 1.0  1-(2-Anihobenzoyl)naphthilane 12-Dibenzofluoren-7-none 1.0  1-(2-Anihobenzoyl)-2-methylinaphthilane 12-Dibenzofluoren-12-one 12-Dimenzofluoren-12-none 1.2-Dimenzofluoren-13-one		•	ting-3', I'-dimethnxybenzaphenone	11-Chrysoftuorenone	Chacosh, nzoos, ou	. e1	75, 194
1.16 and the contraction of the			ոzոչ1-2-ոորիլՈւյիյուսու ԱրտերգիրոշույիդորիլՈւրի	11-Chrysofluorenone	Aq. HCl	13	<u>1</u> 2 1
2-(2'-Anlinobenzoyl)naphthilinene (-). Adi-hilosopia (-). Adi-hilosopi		3-11-6	nzoyl-2-naphthylamine	11-Benzol bjutoren-11-one 7-Benzolejfuoren-7-one	Aq. HCi	Traces	79
1-(2'-Aminobenzoyl)-2'-methymaputamore 5-Methoxy-11-chrysofthorenone Aq. IICl 1-(2'-Aminobenzoyl)-4-methymphthalene 12-Dibenzopbhfluoren-12-one Aq. IICl 3-(2'-Mopthoyl)-2-maphthymmine 12-Dibenzopbhfluoren-12-one Aq. IICl 1-Amino-2-(2',5'-alimethylbenzoyl)anthraquinone 0,12-Dimethylbenzophylog.33-olfluoren-15-01-0-0-0-0-0-0-0-0-0-0-0-0-0-0-0-0-0		61	Andnobenzoyl)naphthalene	6.Methyl-7-benz[de]anthracene-7-one	Ad. HCl	2 10	57
1-(2'-Anunodenzoy)-1-metrosylamine 3-(2'-Nnphthoyl)-2-naphthylmine 1-Aq. H <sub>2</sub> SO <sub>4</sub> , Cu 5-(2'-Nnphthoyl)-2-naphthylmine 5-3 13-trione 5-3 13-trione			.Aminobenzoyl)-g-methymaphthalene	5-Mellioxy-11-chrysoffuorenone	Ag. Chacolan, free	20	75
			Aninopenzoy 17-1 me more mer. Naphthoyl)-2-naphthylmmine	12-Dibenzolbhistuoren-12-one	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	52	105
			nno-2-(2.5'-dlmethylbenzoyl)antiiraquinone	5,8,13-trione			

. These yields are hased on the isolated diazonium fluoborate; the other yields in the table are based on the amine. Note: References 104-225 arollsted on pp. 460-462.

## TABLE IX PHENANTHRIDONES

# Numbering System for Phenanthridone

) 9
, , , ,
Aq. NaOH
Dioxane, H2SO4, H3TO2, Cu
Acetone, H <sub>2</sub> SO <sub>4</sub> , Cu Acetone, HBF., Cu*
done done
3-Bromo-5-ethyl-6(5)-phenanthridone 2.5-Dimethyl-6(5)-phenanthridone Acetone, Cu*
2-Methyl-9-carbomethoxy-6(5)-phenanthridone Aq. H2SO4 or acetone, Cu*
2.4.5-Trimethyl-6(5)-phenanthridone 5-Ethyl-3-methyl-6(5)-phenanthridone
يو
5-Benzyl-6(5)-phenanthridone Aq. acid

The crystalline diazonium saft was used.
The yield was the same in the presence or absence of copper,

### TABLE X

# APORPHINE DERIVATIVES

The Chemical Abstracts name is 6-methyl-5,6,6a,7totrahydro-4-dibenzolde,glquinoline, and the numtotrahydro-farts at aporphine C5.

Product		Product	Procedure	Yield, %	Yield, % Reference
Formula	Starting Amine Starting Allowers 9 3.4-	ւրիկոշ	Aq. CII3OII, II2SO4	<b>21</b>	09
Cullis	1-(2)-Aninobenzyly-6-friency reneway 11-29- tetrahydrolaoquinolline 1-4-1-4-1-4-1-4-1-4-1-4-1-4-1-7-3-1-1-1-1-4-1-1-1-1-4-1-1-1-1-1-1-1-1-1	Aporphine	Aq. HCl, Cu	00	109
(1,111,15)		nedloxyaporphine	Aq. CH3OH, H2SO4	2:1	50, 51
C <sub>14</sub> II <sub>17</sub> NO <sub>2</sub>	1,2,3,4-(etralytroleoptinolino 1,2,3,4-(etralytroleoptinolino 1-(2,5,hilino-4',5-methyloredloxybenzoyl)-6,7- methylonedloxy-2-methyl-1,2,3,4-(etralydroleo-	2,3,5,6-Bis-methylenedloxy-12-ketoaporphine Aq. CII3OU, H2SO4, Cu	А <b>q. СИ<sub>3</sub>ОП, И<sub>2</sub>SO<sub>4</sub>, С</b> и	30	200
5	quindine quindine 1.0%, nino-5, methoxybenzyl)-2-methyl-6,7-	2-Methoxy-5, 6-methylenedloxyaporphine	$\Lambda_{\rm q}$ . ${\rm CH_3OH}$ , ${\rm H_2SO_4}$	20	201, 202
C19 H19-703	1.2., nulno-4. methoxy 1.2.3. 4-tetrahydrolsoquinoline	3-Methoxy-5,6-methylenedioxyaporphine	Aq. CH30H, H2SO4	22	201, 203
	2-nethyl-1,2,3, 4-tetrahydrolsoqulnollne 1-(2., Annino-3-methoxybenzyl)-6,7-methylenedloxy- 4-Methoxy-5,6-methylenedloxyaporphine		Aq. CH <sub>3</sub> OH, H <sub>2</sub> SO <sub>4</sub>	15	204
C.M.NO.	2-methyl-1,2,3,4-tetrahydrolsoqulnollno 1-(2'-Antho-3',4'-dlmethoxybenzyl)-2-methyl-	3,4.Dlmethoxyaporphine	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu	40	205, 21
	1.2,3,4-tetrabydrolsoqulnollne 1-(2'-Aminobenzyl)-2-methyl-6,7-dimethoxy-	5,6-Dlmethoxyaporphine	Aq. CH <sub>3</sub> OH, H <sub>2</sub> SO <sub>4</sub> Aq. H <sub>3</sub> SO <sub>4</sub> , Cu	15 10	206 206
C. II. NO.	1,2,3,1-tetrahydrolsoqulnollne 1,2,2,1,nino-1,5'-dlmethoxybenzyl)-2-methyl-6,7-	2,3-Dlmethoxy-5,6-methylenedloxyaporphlne	Aq. H2SO4, Cu	15	207
11 01	methylenedloxy-1,2,3,4-tetrahydrolsoqulnollne 1-(2-Amho-3',4'-dlmethoxybenzyl)-2-methyl-6,7-	3,4-Dimethoxy-5,6-methylenedloxyaporphine Aq. CH3CH, H2SO4	Аq. СН <sub>3</sub> СН, Н <sub>2</sub> SO <sub>4</sub>	25	208, 209
	methylenedloxy-1,2,3,4-tetrahydrolsoqulnollno 1-(2-Aniho-4',5-methylenedloxybenzyl)-6,7- dlmethoxy-2-methyl-1,2,9,4-tetrahydrolsoqulnollno	5,6-Dimethoxy-2,3-methylenedloxyaporphine ${\rm Aq.H_2SO_4.Cu}$	Αη, <b>Π</b> 250 <sub>4</sub> , Cu	25	210

C. H. NO.	1.(2'-Amino-3',4'-dimethoxybenzyl)-2-methyl-	3,4,6-Trincthoxyaporphine	Aq. CII3OII, II2SO4	ı	211
		3,5,6-Trimethoxyaporphine	Aq. CH <sub>3</sub> OH, H <sub>2</sub> SO <sub>4</sub>	24	212
οχ. 2	xy-6-	nethoxy-2,3-methylenedloxy-	Λη. H <sub>2</sub> SO <sub>4</sub> , Cu	15	213
F		nethoxy-2,3-methylenedloxy-	Λη. Η <sub>2</sub> SO <sub>4</sub> , Cu	20	214
C. Ila.No.		aporphino 2,3,5,G-Tetramethoxy-12-ketoaporphine	Aη. CH3OH, H2SO4, Cu	30	200
C. H. NO.		2,3,5,6-Tetramethoxyaporphine (glaucine)	Αη. <b>H</b> <sub>2</sub> SO <sub>4</sub> , Cu	1	14, 55
•		2,3,6,7.Tetramethoxyaporphine	Aq. CH30H, H2SO4	25	215
	nethoxy-	3,4,5,6-Tetramethoxyaporphine	Aq. H <sub>2</sub> SO <sub>4</sub> , Cu Aq. CH.OH. H <sub>2</sub> SO,	35 15	216 217
	2-inctry-1/2/3/1-tetranythenxylanxylanxyl-1/2/3/10/10/2/3/1-tetranythenxylanxylanxylanxylanxylanxylanxylanxyla	3, 1, 6, 7-Tetramethoxyaporphine	Aq. CH3OH, H2SO4	25	215
J.S. HILL	Craft (1874) 4 1.22. Antender Caretamine Branching through the Craft (1874) 4 1.22. Antender Caretamine Branch (1885) 4 1.42. Antended Section 18 1.43. 18 1.44. 18 1	3-Acetamino-4,5,0-trimethoxyaporphine	Aq. H <sub>2</sub> SO <sub>4</sub> . Cu	က	218
rull,50,	<u></u>	3-Ethoxy-5,6-dimethoxy-10-ethylnoraporphine Cu	Cu	11	219
Cultino	÷	3-Ethoxy-2,5,6-trhnethoxyaporphine	Аq. СН <sub>3</sub> ОН, Н <sub>2</sub> SO <sub>4</sub>	27 crude	220
	1-(2'-Antre-F,5'-diretboxybenzy)-7-ethoxy-6- netboxy-2-nethal-1,2,3,4-tetralydrol-compoline	5-Ethoxy-2.3,6-telmethoxyaporphine	$A\eta$ . $CH_3OH$ , $H_2SO_4$	50	220
Chilliano		2,5-Diethoxy-3,6-dimethoxyaporphine	$A\eta$ . С $H_3OH$ , $H_2SO_4$	5-10	221
	1-(25 Unino-3'-ethoxy-4'-methoxybenzyl)-6-ethoxy- 7-methoxy-2-methyl-1.2.3, 1-tetrahydrolsoquinoline	2,6-Diethoxy-3,5-dlmethoxyaporphine	$A\eta$ . CH $_3$ OH, H $_2$ SO $_4$	10	221
	1(2) Antho-55 etbaxy-Conethoxybenzyl, 6,7-di- methoxy-2-abyl-1,2,3,1-feffallydrelsoquinolline	2-Ethoxy-3,5,6-frlmethoxy-10-ethylnorapor- phine	$\Lambda$ q. С $\mathrm{H}_{3}\mathrm{OH}$ , $\mathrm{H}_{2}\mathrm{SO}_{4}$	23	222
CnII, NO,	methery-2-chyl-2-4-tetrahydrotsomine feet Vriteval 1, almost and	3. Ethoxy-2,5,6-trimethoxy-10-cfhylnor- aporphine	Aη. CΠ <sub>3</sub> OH, H <sub>2</sub> SO <sub>4</sub>	22-24	222
"unayo	J. C. Hilliydel, equipolite (heavy) consylve-bensylvey. J. C. Frifax C. Constantian (heavy) and the constantian (h	d-Penzyloxy-3,4-dimethoxy-10,11- dehydronoraporphine	Αη. H <sub>2</sub> SO <sub>4</sub> , Cu	ī	253
,	dimethoxys-2 methyl-1.2.3, 4-tetrahydmisequinoline	3-lkazyloxy-2,5,6-trimelhoxyaporphine	Аq. СН <sub>3</sub> ОН, Н <sub>2</sub> SO <sub>4</sub>	64 crude	¥ 667

### TABLE XI

### SULTONES AND SULTAMS

Molecular Formula of Sultone	Corresponding Sulfonic Acid	Yield, %	Reference
C12116C12O3S	4,5'-Dichloro-2'-hydroxybiphenyl-2-sulfonic acid	16*	49 49
C12117C1O3S	5'-Chloro-2'-hydroxybiphenyl-2-sulfonic acid	15	49
C <sub>12</sub> 11,C1O <sub>3</sub> S	5-Chloro-2'-hydroxyhiphenyl-2-sulfonie acid	80	49
$C_{12}H_8O_3S$	2'-Hydroxybiphenyl-2-sulfonic acid	52	_
C <sub>13</sub> II <sub>9</sub> ClO <sub>3</sub> S	5-Chloro-2'-hydroxy-5'-methylbiphenyl-2-sulfonic acid	46	49
C <sub>16</sub> 11 <sub>10</sub> O <sub>3</sub> S	1-(2'-Sulfophenyl)-2-naphthol	50	49
$C_{16}H_{10}O_{3}S$	2-(2'-Sulfophenyl)-1-naphthol	32	49
$C_{17}H_{18}O_3S$	5'-tert-Amyl-2'-hydroxybiphenyl-2-sulfonic acid	23	49
Molecular Formul	a		
of Sultam	Sultams		
C12H2NO2S	Sultam of 2'-amino-2-biphenylsulfonic acid	76†	52
C <sub>13</sub> H <sub>11</sub> NO <sub>2</sub> S	Sultam of 2'-methylamino-2-biplienylsulfonic acid	80†	52
C <sub>16</sub> H <sub>11</sub> NO <sub>2</sub> S	Sultam of 2-(2'-amino-1-naplithyl)-benzenesulfonic acid	90‡	52

- . The sultones were all prepared by heating the diazonium salt in the presence of copper powder
- † The sultam was prepared by heating the aqueous solution of the diazonium salt.
- . The sultam was prepared by pyrolysis of the triazene in the presence of sodium hydroxide and copper powder.

### References to Tables I-XI

- 104 Taylor and Hobson, J. Chem. Soc., 1936, 181.
- 105 Ruggli and Dinger, Helv. Chim. Acta, 24, 173 (1941).
- 106 Barber and Stickings, J. Chem. Soc., 1945, 167.
- 107 May and Mosettig, J. Org. Chem., 11, 627, 631 (1946).
- 108 Schofield and Swain, J. Chem. Soc., 1949, 2393.
- 109 Nylén, Ber., 53, 158 (1920).
- 110 May and Mosettig, J. Org. Chem., 11, 441 (1946).
- 111 Hey and Osbond, J. Chem. Soc., 1949, 3172.
- 112 Mosettig and Burger, J. Am. Chem. Soc., 52, 2988 (1930).
- 113 Konovalova, Yunusov, and Orekhov, Bull. soc. chim. France, [5] 6, 1479 (1939);
- J. Gen. Chem., U.S.S.R., 9, 1507 (1939) [C. A., 34, 2852 (1940)].
  - 114 Werner and Scherrer, Ann., 322, 135 (1902).
  - 115 May, J. Am. Chem. Soc., 69, 717 (1947).
  - 118 Akin, Stamatoff, and Bogert, J. Am. Chem. Soc., 59, 1268 (1937).
  - 117 Mayer and English, Ann., 417, 60 (1918).
  - 116 Hill, Short, and Stromberg, J. Chem. Soc., 1937, 937.
  - 119 Higginbottom, Hill, and Short, J. Chem. Soc., 1937, 263.
  - 120 Hill, Short, Stromberg, and Wiles, J. Chem. Soc., 1937, 510.
  - 111 Holmes, Lee, and Mooradian, J. Am. Chem. Soc., 69, 1998 (1947).
  - 112 Knorr and Hörlein, Ber., 40, 2010 (1907).
  - 123 Rapson and Robinson, J. Chem. Soc., 1935, 1541.
  - 124 Akin and Bogert, J. Am. Chem. Soc., 59, 1564 (1937).
  - 113 Shirai, J. Pharm. Soc. Japan, 63, 517 (1943) [C. A., 45, 3401 (1951)].
  - 116 Knorr and Hörlein, Ber., 42, 3497 (1909).
  - 117 Schlittler and Müller, Helv. Chim. Acta, 31, 1119 (1948).
  - 113 Cassaday and Bogert, J. Am. Chem. Soc., 61, 3055 (1939).
  - 114 Mayer and Oppenheimer, Ber., 51, 510 (1918).
  - 124 Weitzenblock and Lieb, Monatsh., 33, 549 (1912).

```
<sup>131</sup> Kondo and Ochiai, J. Pharm. Soc. Japan, No. 539, 17 (1927) [C. A., 22, 4531 (1928)];
Ann., 470, 224 (1929).
 132 Goto and Sudzuki, Bull. Chem. Soc. Japan, 4, 163 (1929) [C. A., 24, 122 (1930)].
 133a Hewett and Martin, J. Chem. Soc., 1940, 1396.
 133b Wolf, J. Am. Chem. Soc., 75, 2073 (1953).
 134 Cassaday and Bogort, J. Am. Chem. Soc., 61, 2461 (1939).
 135 Sharp, J. Chem. Soc., 1936, 1234.
 136 Buchanan, Cook, and Loudon, J. Chem. Soc., 1944, 325.
 137 Rapoport, Williams, and Cisnoy, J. Am. Chem. Soc., 73, 1414 (1951).
 138 Barton, Cook, and Loudon, J. Chem. Soc., 1945, 176.
 139 Gulland and Virden, J. Chem. Soc., 1928, 1478.
 140 Rapoport, Allen, and Cisney, J. Am. Chem. Soc., 77, 670 (1955).
 141 Briggs and Wilson, J. Chem. Soc., 1941, 500.
  142 Gulland and Virden, J. Chem. Soc., 1928, 921.
  143 Späth and Tharrer, Ber., 66, 583 (1933).
  144 Fieser and Kilmer, J. Am. Chem. Soc., 62, 1354 (1940).
  145 Hewett, J. Chem. Soc., 1938, 1286; 1940, 293.
  146 Rajagopalan, Proc. Indian Acad. Sci., 13A, 566 (1941) [C. A., 35, 7965 (1941)].
  147 Barger and Silberschmidt, J. Chem. Soc., 1928, 2919.
  148 Cook and Stephenson, J. Chcm. Soc., 1949, 842.
  149 von Braun and Zobel, Ber., 56, 2142 (1923).
  150 Cook, J. Chem. Soc., 1933, 1592.
  151 Weitzenböck and Klinger, Monatsh., 39, 315 (1918).
  152 Waldmann, Spiegel, and Kunz, J. prakt. Chem., [2] 135, I (1932).
  153 Waldmann and Pitschak, Ann., 527, 183 (1937).
  154 Hornig, J. Am. Chem. Soc., 74, 4572 (1952).
  155 Cassaday and Bogert, J. Am. Chem. Soc., 61, 3058 (1939).
  156 Windaus, Jensen, and Schramme, Ber., 57, 1875 (1924).
  157 Tucker and Whalley, J. Chem. Soc., 1952, 3187.
  158 Stubbs and Tucker, J. Chem. Soc., 1954, 227.
  159 Hawkins and Tucker, J. Chem. Soc., 1950, 3286.
   160 Tucker and Whalley, J. Chem. Soc., 1949, 632.
   161 Stubbs and Tucker, J. Chem. Soc., 1951, 2936.
   162 Beaton and Tucker, J. Chem. Soc., 1952, 3870.
   163 Bremer, Ann., 514, 279 (1934).
   184 Waldmann and Back, Ann., 545, 52 (1940).
   165 Ullmann, Kogan, and Deletra, Ann., 332, 82 (1904).
   166 Storrie and Tucker, J. Chem. Soc., 1931, 2255.
   167 Campbell and MacLean, J. Chem. Soc., 1942, 504.
   168 Ullmann and Illgen, Ber., 47, 380 (1914).
   169 Hunter and Darling, J. Am. Chem. Soc., 53, 4183 (1931).
   170 Macrae and Tucker, J. Chem. Soc., 1933, 1520.
   171 Nelmes and Tucker, J. Chem. Soc., 1933, 1523.
   172 Tucker, J. Chem. Soc., 1926, 3033.
   173 Plant and Tomlinson, J. Chem. Soc., 1932, 2188.
   174 Burton and Gibson, J. Chem. Soc., 125, 2501 (1924).
   175 Preston and Tucker, J. Chem. Soc., 1943, 659.
   178 McCombie, MacMillan, and Scarborough, J. Chem. Soc., 1931, 529.
    177 Cullinane, J. Chem. Soc., 1930, 2267.
    178 Graebe and Ullmann, Ber., 29, 1876 (1896).
    179 Cullinanc, Davies, and Davies, J. Chem. Soc. 1936, 1435.
    Davies, James, Middleton, Porter, J. Chem. Soc., 1955, 1565.
    181 Block, Jr., J. Am. Chem. Soc., 72, 5641 (1950).
    162 Neumoyer and Amstutz, J. Am. Chem. Soc., 66, 1680 (1944).
    163 Guyot and Granderye, Bull. soc. chim. France, [3] 33, 198 (1905),
    184 Haller and Guyot, Bull. soc. chim. France, [3] 25, 750 (1901).
```

- 185 Ullmann and Broido, Ber., 39, 356 (1906).
- 186 Huntress, Pfister, and Pfister, J. Am. Chem. Soc., 64, 2845 (1942).
- 187 Ullmann and Mallett, Ber., 31, 1694 (1898).
- 188 Chardonnens and Lienert, Helv. Chim. Acta, 32, 2340 (1949).
- 189 Chardonnens and Perriard, Helv. Chim. Acta, 28, 593 (1945).
- 190 Lifschitz, Rec. trav. chim., 54, 397 (1935).
- 191 Chardonnens and Würmli, Helv. Chim. Acta, 29, 922 (1946).
- 192 Mulholland and Ward, J. Chem. Soc., 1954, 4676.
- 193 Reichert, Arch. Pharm., 270, 551 (1932) [C. A., 27, 717 (1933)].
- 194 Graebe, Ber., 29, 826 (1896).
- 195 Schaarschmidt and Herzenberg, Ber., 53, 1807 (1920).
- 196 Heacoek and Hey, J. Chem. Soc., 1952, 4059.
- 197 Pictet and Gonset, Arch. sci. phys. nat. Genève, [4] 3, 37 (1897) (Chem. Zentr., 1897, I, 413).
  - 198 Mitsuhashi, J. Pharm. Soc. Japan, 63, 177 (1943) [C. A., 45, 628 (1951)].
  - 199 Gadamer, Oberlin, and Schoeler, Arch. Pharm., 263, 81 (1925).
  - 200 Schlittler and Lindenmann, Helv. Chim. Acta, 32, 1880 (1949).
  - <sup>201</sup> Faltis, Wagner, Adler, Bcr., 77, 686 (1944).
  - <sup>202</sup> Marion, J. Am. Chem. Soc., 66, 1125 (1944).
  - <sup>203</sup> Schlittler, Helv. Chim. Acta, 15, 394 (1932).
  - 204 Barger and Schlittler, Helv. Chim. Acta, 15, 381 (1932).
  - <sup>205</sup> Späth and Hromatka, Ber., 62, 325 (1929).
  - 206 Gulland and Haworth, J. Chem. Soc., 1928, 581.
  - <sup>207</sup> Haworth, Perkin, Jr., and Rankin, J. Chem. Soc., 127, 2018 (1925); 1926, 29
  - 208 Gulland and Haworth, J. Chem. Soc., 1928, 1132.
  - 209 Spath and Hromatka, Ber., 61, 1334 (1928).
    - 210 Kitasato and Shishido, Ann., 527, 176 (1937).
    - 211 Gulland and Haworth, J. Chem. Soc., 1928, 2083.
    - 212 Goto, Ianba, and Nozaki, Ann., 530, 142 (1937).
    - <sup>213</sup> Shishido, Bull. Chem. Soc. Japan, 12, 150 (1937) [C. A., 31, 5802 (1937)].
    - <sup>214</sup> Shishido, Bull. Chem. Soc. Japan, 12, 419 (1937) [C. A., 32, 944 (1938)].
    - 215 Callow, Gulland, and Haworth, J. Chem. Soc., 1929, 658.
    - 216 Spath and Hromatka, Bcr., 61, 1692 (1928).
    - <sup>217</sup> Gulland and Haworth, J. Chem. Soc., 1928, 1834.
    - <sup>218</sup> Robinson and Shinoda, J. Chem. Soc., 1926, 1987.
    - 219 Goto and Shishido, Ann., 539, 262 (1939).
    - 220 Manske, Charlesworth, and Ashford, J. Am. Chem. Soc., 73, 3751 (1951).
    - 221 Schlittler, Ber., 68, 988 (1933).
    - 222 Barger, Eisenbrand, Eisenbrand, and Schlittler, Ber., 68, 450 (1933).
    - 223 Kondo and Ishiwata, Ber., 64, 1533 (1931).
    - 224 Douglas and Gulland, J. Chem. Soc., 1931, 2893.
  - <sup>225</sup> Govindachari and Arumugam, J. Sci. Ind. Research India, 14B, 250 (1955) [C. A., 50, 342 (1956)].

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